A COMPARATIVE STUDY OF RAMIPRIL AND TELMISARTAN ON INFLAMMATORY MEDIATED RESPONSE AND ANTIHYPERTENSIVE EFFICACY IN ACUTE CORONARY SYNDROME PATIENTS

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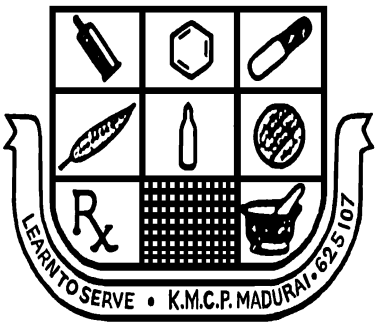

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CERTIFICATE

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF RAMIPRIL AND TELMISARTAN ON INFLAMMATORY MEDIATED RESPONSE AND ANTIHYPERTENSIVE EFFICACY IN ACUTE CORONARY SYNDROME PATIENTS"** submitted by **Mr. ARUN. R** to The Tamilnadu Dr. M.G.R Medical university, Chennai**,** in partial fulfillment of the requirement for the award of **Master of Pharmacy in Pharmacy Practice**, at **K.M.College of Pharmacy,** Uthangudi, Madurai-625107. It is a bonafide work carried out by him under my guidance and supervision during the academic year 2011 – 2012. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other universities.

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INTRODUCTION

Coronary heart disease is one of the most common causes of death worldwide and is the leading cause of death among men and women. In 1990, ischemic heart disease accounted for 6.3 million deaths worldwide. The age standardized incidence varies among and within countries. There were about 1.6 million hospital discharges for ACS in the US in 2003. About 30% of ACS patients have STEMI. In industrialized countries the annual incidence of unstable angina is in the region of 6 cases per 10,000 people. The incidence of ACS increases with age with a higher incidence among men until the age of 70. Women who are 15 years postmenopausal are equally likely as men to develop ACS. About 90% of patients with coronary heart disease report at least 1 of the major risk factors, including cigarette smoking, dyslipidemia, hypertension, diabetes, and abdominal obesity[1] .

Patients in India who have acute coronary syndromes have a higher rate of STEMI than do patients in developed countries. Since most of these patients were poor, less likely to get evidence-based treatments, and had greater 30-day mortality, reduction of delays in access to hospital and provision of affordable treatments could reduce morbidity and mortality[2].

Acute coronary syndrome occurs when an atherosclerotic plaque ruptures, leading to thrombus formation within a coronary artery, or coronary thrombosis. Patients who develop acute coronary syndrome symptoms such as chest pain and diaphoresis require timely evaluation to determine the cause. ACS refers to a range of acute myocardial ischaemic states, which include**:**

- ST-elevation ACS (STE-ACS): patients present with acute chest pain and persistent (>20 minutes) ST-segment elevation. Most of these patients will develop an ST-elevation MI (STEMI).
- Non-ST-elevation ACS (NSTE-ACS)**:** patients present with acute chest pain but without persistent ST-segment elevation. The ECG shows persistent or transient ST-segment depression or T-wave inversion, flat T waves, pseudo-normalisation of T waves, or no ECG changes at presentation. NSTE-ACS is further divided into:

  *Unstable angina: normal troponin levels

  *Non-ST-elevation MI (NSTEMI)**:** a rise in troponin levels.

COMPLICATIONS

- Acute myocardial infarction.
- Cardiogenic shock.
- Ischaemic mitral regurgitation.
- Supraventricular arrhythmias: rare complication of ischaemia but may precipitate ischaemic events.
- Ventricular arrhythmias: simple and complex premature ventricular contractions and nonsustained ventricular tachycardia.
- Atrioventricular nodal blockade: usually transient in setting of reversible ischaemia (treatment is guided by location of block and haemodynamic stability)[3].

EPIDEMIOLOGY

The incidence of ACS is clearly associated with increasing age. In 2010, the estimated number of incident cases of ACS increased from approximately 167,770 in those aged less than 50 years to about 356,000 in those age 80 years or more. On average, there are 1.8 cases of incident ACS in men for every one case in women. The exception to this is pattern in Italy where there are only 1.1 cases of incident ACS in men for every one case of incident ACS in women.

Datamonitor estimates that in the US and the five major EU markets, 36% of cases of ACS are STEMI, 34% are NSTEMI, and 30% are UA. In Japan, Datamonitor estimates that 51% of cases of ACS are STEMI, 10% are NSTEMI, and 39% are UA[4].

PATHOPHYSIOLOGY

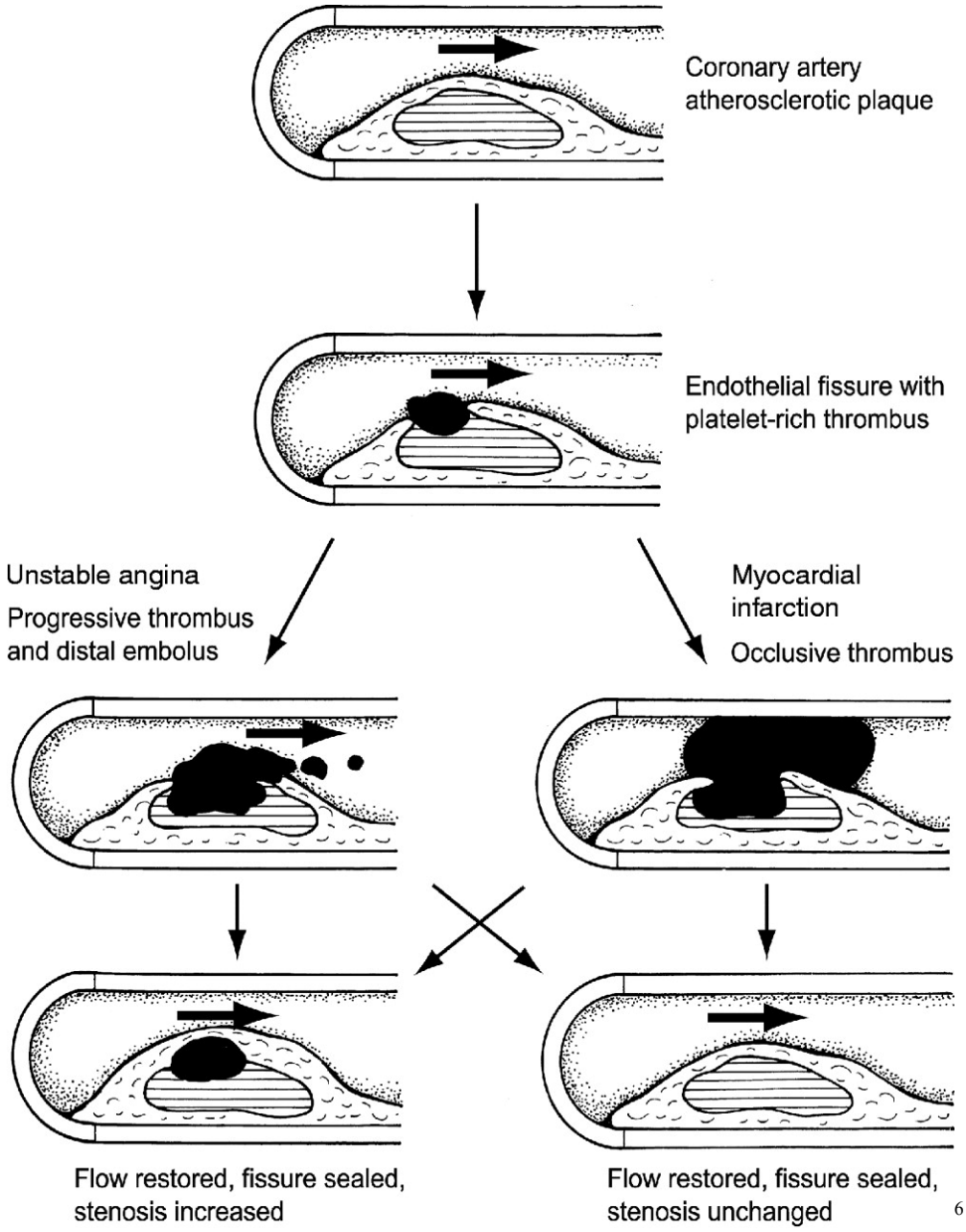
The coronary arteries become stenosed with age by the deposition of lipid-rich atheroma in the sub-endothelial layer. There are a number of factors that have been shown to encourage the development of premature coronary disease. These include smoking, hypertension, hypercholesterolaemia, diabetes mellitus, obesity and a family history. Atherosclerotic plaque formation commences when macrophages are attracted to the site of vessel injury. A meshwork of extracellular matrix proteins surrounds a lipid core, the latter resulting from the incorporation of bloodstream lipids by activated macrophages. Deposits tend to accumulate around bifurcations of the arteries and result in reduced blood flow when there is >50% diameter reduction. The

medial muscle coat of the coronary arteries is under tonic contraction, mediated by the autonomic nervous system, which can affect changes in diameter by constriction or dilatation. The imbalance between coronary blood flow and myocardial demand produces ischaemia, which is manifest as angina. Thus, although in most cases angina occurs in association with increased heart work during physical exercise, it can also occur as a result of autonomic changes. For example, angina is classically worse in cold weather because changing autonomic tone causes coronary artery constriction. When angina only occurs with exercise and it is reproduced by the same degree of exercise, this is called chronic stable angina.

The pattern of angina may change with time over years, but can occur more abruptly over days. This is usually attributable to the development of a thrombus on the surface of an atheromatous plaque within the artery after plaque rupture or fissuring. Plaque rupture exposes a mixture of lipid and collagen, both of which promote the development of thrombus by platelet adherence and activation, as well as activation of the coagulation cascade. There are many factors involved in the adherence and activation of platelets ,but the final common pathway of 'white thrombus' is the activation of glycoprotein (GP) IIb/IIIa receptors, the platelet surface membrane receptor for fibrinogen. Fibrinogen cross-links develop between activated GP IIb/IIIa receptors, leading to the formation of a platelet thrombus. Thrombus development is rapid and so symptom deterioration is sudden.

When the pattern changes so that it occurs more easily than previously, but still only on exercise, it is called crescendo angina. When angina occurs at rest this means that the myocardium is ischaemic even in the absence of an increase in workload and implies critical myocardial perfusion. This constitutes the diagnosis of unstable angina (UA). It is not necessary to have a severe artery stenosis in order to develop a thrombus. In the majority of cases it is the result of endothelial fissuring on the site of a non-significant stenosis[5].

Processes involved in reduction of blood flow during an acute coronary event.



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ETIOLOGY

Acute coronary syndrome is caused primarily by atherosclerosis. Most cases of ACS occur from disruption of a previously nonsevere lesion (an atherosclerotic lesion that was previously hemodynamically insignificant yet vulnerable to rupture). Elevated demand can produce ACS in the presence of a high-grade fixed coronary obstruction, due to increased myocardial oxygen and nutrition requirements, such as those resulting from exertion, emotional stress, or physiologic stress (eg, from dehydration, blood loss, hypotension, infection, thyrotoxicosis, or surgery). ACS without elevation in demand requires a new impairment in supply, typically due to thrombosis andor plaque hemorrhage.

The major trigger for coronary thrombosis is considered to be plaque rupture caused by the dissolution of the fibrous cap, the dissolution itself being the result of the release of metalloproteinases (collagenases) from activated inflammatory cells. This event is followed by platelet activation and aggregation, activation of the coagulation pathway, and vasoconstriction. This process culminates in coronary intraluminal thrombosis and variable degrees of vascular occlusion. Distal embolization may occur. The severity and duration of coronary arterial obstruction, the volume of myocardium affected, the level of demand on the heart, and the ability of the rest of the heart to compensate are major determinants of a patient's clinical presentation and outcome. Anemia and hypoxemia can precipitate myocardial ischemia in the absence of severe reduction in coronary artery blood flow.

A syndrome consisting of chest pain, ischemic ST-segment and T-wave changes, elevated levels of biomarkers of myocyte injury, and transient left ventricular apical ballooning (takotsubo syndrome) has been shown to occur in the absence of clinical CAD, after emotional or physical stress. The etiology of this syndrome is not well understood but is thought to relate to a surge of catechol stress hormones and/or high sensitivity to those hormones[7].

Patients are more likely to develop coronary heart disease if they:

- smoke cigarettes regularly
- have high blood cholesterol level
- have high blood pressure
- do not get enough exercise
- are diabetic
- have an unhealthy diet
- are overweight
- drink too much alcohol

CLINICAL PRESENTATION

Most Common Symptoms of ACS include:

- Chest pain due to the heart muscle not getting enough blood, called angina, this discomfort may feel like pressure, burning or tightness. It can occur during exercise, periods of emotional stress, after eating a large meal, or even while resting.

- Pain in other areas; typically the upper arm or jaw.
- Nausea.
- Vomiting.
- Shortness of breath.
- Sudden, heavy sweating.
- Light-headedness[8].

DIFFERENTIAL DIAGNOSIS

- Cardiovascular: ST-segment elevation infarction, acute pericarditis, myocarditis, aortic stenosis, aortic dissection, pulmonary embolism.
- Respiratory: pneumonia, pneumothorax.
- Gastrointestinal: oesophageal spasm, oesophagitis, gastro-oesophageal reflux, acute gastritis, cholecystitis, pancreatitis.
- Musculoskeletal chest pain.

INVESTIGATIONS

It is essential to exclude a myocardial infarction with ST elevation for which immediate thrombolysis is indicated.

12-lead ECG:

- To confirm a cardiac basis for presentation and may show pre-existing structural or ischaemic heart disease (e.g. left ventricular hypertrophy, Q waves).
- A normal or unchanged ECG does not exclude the possibility that chest pain is ischaemic in origin.
- Changes that may be seen during episodes of angina include transient ST-segment elevations (fixed changes suggest acute infarction).
- In unstable angina (and non-Q wave infarction) the ECG typically shows T-wave inversion or ST-segment depression, but the ECG may be normal if some time has elapsed since the last episode of pain.

Cardiac enzymes:

- Within the first 6 hours, the sensitivity of troponins is superior to CK-MB for the detection of myocardial infarction.
- Troponin I and T become detectable in serum 3-6 hours after infarction, peak at 12-24 hours, and remain raised for up to 14 days.Troponins are therefore usually tested 6 and 12 hours after the onset of pain.
- In patients with unstable angina, minor troponin elevations may identify patients at risk for subsequent cardiac events and death. Elevated troponin levels indicate an increased risk of mortality in both the short-term and long-term. Patients with chest pain and elevated troponin levels should remain in hospital for further assessment, including an inpatient coronary angiogram.

Full blood count(FBC):

FBC may be useful in patients with suspected anaemia and as a baseline in view of use of anticoagulants; blood glucose, renal function and electrolytes.

Blood glucose:

Hyperglycaemia is common in people admitted to hospital with ACS. Hyperglycaemia at the time of admission with ACS is a powerful predictor of poorer survival and increased risk of complications while in hospital, regardless of whether or not the patient has diabetes.

Echocardiography:

Echocardiography often demonstrates wall motion abnormalities due to ischaemia. May be useful in identifying precipitants for ischaemia, e.g. ventricular hypertrophy and valvular disease.

Chest X-Ray(CXR):

CXR may show complications of ischaemia, e.g. pulmonary oedema, or explore alternative diagnoses, e.g. pneumothorax, aortic aneurysm.

Cardiac Magnetic Resonance (CMR) Imaging:

Cardiac magnetic resonance imaging can be useful for the assessment of function and perfusion, and the detection of scar tissue. CMR can also be useful to exclude or detect ACS, assess myocardial viability and to detect myocarditis.

Coronary Angiography:

Coronary angiography provides information on the presence and severity of coronary artery disease and therefore remains the gold standard[9].

NON PHARMACOLOGICAL INTERVENTION

On admission, patients had poor knowledge of cardiovascular risk factors and recommended lifestyle modifications, especially concerning diabetes, hypertension, and diet. After completing the rehabilitation programme, significantly higher percentage of patients gave correct answers to questions concerning diabetes and cholesterol-rich diet as cardiovascular risk factors, and substitution of vegetable fat for animal fat as a lifestyle modification, and significantly higher proportion of patients gave the correct value for elevated systolic blood pressure.

Steps to prevent acute coronary syndrome or to prevent acute coronary syndrome are quitting smoking, have exercise most days of the week for at least 30 minutes each time, taking a healthy diet, regular check up of blood pressure and cholesterol levels, maintain a healthy weight, managing stress [10].

DRUG THERAPY

The treatment of patients with non-ST-segment elevation ACS is directed to alleviate pain and anxiety, prevent recurrences of ischaemia and prevent or limit progression to acute myocardial infarction. Treatment includes antithrombotic treatment, as well as coronary angiography followed by revascularisation if appropriate.

Immediate management of a suspected ACS

- Arrange urgent hospital admission
- Resuscitation as required.
- Pain relief: glyceryl trinitrate (GTN) and/or an intravenous opioid (use an antiemetic with opioids).
- Single loading dose of 300 mg aspirin unless the person is allergic.
- A resting 12-lead ECG - but don't delay transfer to hospital.
- Assess oxygen saturation, using pulse oximetry before hospital admission if possible. Give oxygen if oxygen saturation (SpO_2) is less than 94% with no risk of hypercapnic respiratory failure; aim for SpO_2 of 94-98% (aim for 88-92% for people with chronic obstructive pulmonary disease).

Anti platelet and anticoagulant therapy

Aspirin:

Single 300-mg loading dose to all patients, unless contra-indicated, and continue indefinitely. Consider clopidogrel monotherapy for patients with aspirin hypersensitivity.

Clopidogrel:

- Offer a 300-mg loading dose to patients with a predicted 6-month mortality of more than 1.5% and no contra-indications (such as increased bleeding risk).

- Offer a 300-mg loading dose to all patients with no contra-indications who may undergo PCI within 24 hours of admission.
- Continue standard dose for 12 months.
- Consider stopping clopidogrel 5 days before CABG in patients with low risk. For patients at intermediate or higher risk, whether to continue clopidogrel before CABG depends on the balance of ischaemic and bleeding risk.

Prasugrel

Prasugrel in combination with aspirin is recommended as an option for preventing atherothrombotic events in people with acute coronary syndromes having percutaneous coronary intervention, only when:

- immediate primary percutaneous coronary intervention for ST-segment-elevation myocardial infarction is necessary; or
- stent thrombosis has occurred during clopidogrel treatment; or the patient has diabetes mellitus

Ticagrelor

Ticagrelor in combination with low-dose aspirin is recommended for up to 12 months as a treatment option in adults with acute coronary syndromes (ACS) with: STEMI that cardiologists intend to treat with primary percutaneous coronary intervention (PCI); or NSTEMI; or admitted to hospital with unstable angina.

Glycoprotein IIb/IIIa inhibitors:

- Consider **eptifibatide or tirofiban** for patients at intermediate or higher risk if angiography is scheduled within 96 hours of admission.
- Consider **abciximab** as an adjunct to PCI for patients at intermediate or higher risk who are not already receiving a glycoprotein inhibitor (GPI).

Antithrombin therapy :

Anticoagulants are used in the treatment of NSTE-ACS to inhibit thrombin generation and/or activity, thereby reducing thrombus-related events.

- Offer **fondaparinux** to patients without a high bleeding risk unless angiography is planned within 24 hours of admission.

- Offer **unfractionated heparin** as an alternative to fondaparinux if angiography is likely within 24 hours of admission
- Carefully consider the choice and dose of antithrombin in patients with a high bleeding risk.
- Consider unfractionated heparin, with dose adjusted to clotting function, for patients with creatinine above 265 μmol/L.
- Offer systemic unfractionated heparin (50-100 units/kg) in the cardiac catheter laboratory to patients on fondaparinux who are undergoing PCI.
- As an alternative to the combination of a heparin plus a GPI, consider **bivalirudin** for patients who are at intermediate or higher risk, and are not already receiving a GPI or fondaparinux, and are scheduled for angiography within 24 hours of admission.
- As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients undergoing PCI who are at intermediate or higher risk and are not already on a GPI or fondaparinux.

Revascularisation:

- Offer coronary angiography (with follow-on PCI if indicated) within 96 hours of first admission to hospital to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3%) if they have no contra-indications to angiography such as active bleeding or comorbidity) Perform angiography as soon as possible for patients who are clinically unstable or at high ischaemic risk.
- When the role of revascularisation or the revascularisation strategy is unclear, resolve this by discussion involving an interventional cardiologist, cardiac surgeon and other healthcare professionals relevant to the needs of the patient. Discuss the choice of the revascularisation strategy with the patient.
- The proportion of patients with NSTE-ACS undergoing coronary artery bypass surgery during initial hospitalisation is about 10%. The benefit from bypass surgery is greatest when patients can be operated on after several days of medical stabilisation depending on the individual risk.

Other treatments:

- **Nitrates** (sublingual, oral or intravenous): for ongoing pain whilst waiting for more definitive procedures, and may overcome superimposed coronary artery spasm.
- **Beta-blockers** improve outcome and can reduce the severity and frequency of attacks.
- **Calcium antagonists (e.g. diltiazem, verapamil)** are used for patients who cannot tolerate a beta-blocker, or are used in addition to a beta-blocker. Verapamil should not be combined with a beta-blocker.
- **Angiotensin-converting enzyme (ACE) inhibitors** reduce mortality and should be started when the patient is an inpatient unless contra-indicated.

Hyperglycaemia:

- Hyperglycaemia in patients admitted to hospital for an ACS should be managed by keeping blood glucose levels below 11.0 mmol/L while avoiding hypoglycaemia. A dose-adjusted **insulin infusion** with regular monitoring of blood glucose levels should be considered.
- All patients with hyperglycaemia after ACS and without known diabetes should be tested for HbA1c levels before discharge and fasting blood glucose levels no earlier than 4 days after the onset of ACS.

After stabilisation, secondary risk reduction measures should be implemented. These measures include stopping smoking, continued aspirin therapy, management of hypertension if present, statins, ACE inhibitors and beta-blockers.If a patient was stabilised with medical treatment then it is likely they will undergo treadmill exercise testing[11].

Further management

- To detect and quantify inducible ischaemia, consider ischaemia testing before discharge for patients whose condition has been managed conservatively and who have not had coronary angiography.

- Assess left ventricular function in all patients who have had a myocardial infarction and consider assessing left ventricular function in all patients with unstable angina.
- Cardiac rehabilitation: rehabilitation and discharge planning.
- Secondary prevention: management of cardiovascular risk factors with lifestyle changes and drug therapy as indicated[12].

HYPERTENSION

High blood pressure, termed "hypertension," is a condition that afflicts almost 1 billion people worldwide and is a leading cause of morbidity and mortality. More than 20% of Americans are hypertensive, and one-third of these Americans are not even aware they are hypertensive. Therefore, this disease is sometimes called the "silent killer." This disease is usually asymptomatic until the damaging effects of hypertension such as stroke, myocardial infarction, renal dysfunction, visual problems, etc are observed. Hypertension is a major risk factor for coronary artery disease and "heart attacks," which may require coronary artery bypass surgery[13].

Normal blood pressure is defined as an average systolic blood pressure of 120 mm Hg and an average diastolic pressure of 80 mm Hg. Systolic pressure measures the pressure in arteries when your heart beats. Diastolic pressure measures the pressure between beats. Hypertension is defined as an average systolic blood pressure above 140 mm Hg, a diastolic blood pressure above 90 mm Hg, or both[14].

Hypertension has its worst effects on the heart, kidneys, eyes, and brain. High blood pressure is a risk factor for heart attack, stroke, kidney failure, hemorrhages of the retina of the eye, and generalized atherosclerosis (hardening of the arteries all over the body)[15].

The two major types are:

- Primary or essential hypertension, that has no known cause, is diagnosed in the majority of people.
- Secondary hypertension is often caused by reversible factors, and is sometimes curable.

The other types include:

- Malignant Hypertension.
- Isolated Systolic Hypertension
- White Coat Hypertension
- Resistant Hypertension

Primary Hypertension:

This type is also called essential hypertension, and it is by far the most common type of hypertension, and is diagnosed in about 95% of cases. Essential hypertension has no obvious or yet identifiable cause.

Secondary Hypertension:

This may be caused by:

- Kidney damage or impaired function (This accounts for most secondary forms of hypertension.)
- Tumours or overactivity of the adrenal gland
- Thyroid dysfunction
- Coarctation of the aorta
- Pregnancy-related conditions
- Sleep Apnea Syndrome
- Medication, recreational drugs, drinks & food

Malignant Hypertension

This, the most severe form of hypertension, is severe and progressive. It rapidly leads to organ damage. Unless properly treated, it is fatal within five years for the majority of patients. Death usually comes from heart failure, kidney damage or brain haemorrhage. However, aggressive treatment can reverse the condition, and prevent its' complications. Malignant hypertension is becoming relatively rare, and is not caused by cancer or malignancy.

Isolated Systolic Hypertension

In this case the systolic blood pressure is consistently above 160 mm Hg and the diastolic below 90 mm Hg. This may occur in older people, and results from the age-related stiffening of the arteries. The loss of elasticity in arteries, like the aorta, is mostly due to arteriosclerosis. The Western lifestyle and diet is believed to be the root

cause. Latest studies confirm the importance of treating ISH, as it significantly reduces the incidence of stroke and heart disease. Treatment starts with lifestyle modification, and if needed, added drugs.

White coat hypertension

Also called anxiety-induced hypertension, it means blood pressure is only high when tested by a health professional. If confirmed, with repeat readings outside of the clinical setting, or a 24-hour monitoring device, it does not need to be treated. However, regular follow-up is recommended to ensure that persistent hypertension has not developed.

Lifestyle changes like more exercise, less salt and alcohol, no nicotine and weight loss, would be wise. A low fat, high fibre diet, with increased fruit and vegetable intake, will be beneficial.

Resistant Hypertension

If blood pressure cannot be reduced to below 140/90 mmHg, despite a triple-drug regime, resistant hypertension is considered[16].

COMPLICATIONS

- Artery Damage
- Blindness
- Kidney Failure
- Metabolic Syndrome
- Memory Loss
- Aneurysm
- Stroke

EPIDEMIOLOGY

In many countries, 50% of the population older than 60 years has hypertension. Overall, approximately 20% of the world's adults are estimated to have hypertension. The 20% prevalence is for hypertension defined as BP in excess of 140/90 mm Hg. The prevalence dramatically increases in patients older than 60 years. However, approximately 30% of adults are still unaware of their hypertension; up to

40% of people with hypertension are not receiving treatment; and, of those treated, up to 67% do not have their blood pressure (BP) controlled to less than 140/90 mm Hg[17]. Cardiovascular diseases caused 2.3 million deaths in India in the year 1990; this is projected to double by the year 2020. Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India. Indian urban population studies in the mid-1950s used older WHO guidelines for diagnosis (BP > or =160 and/or 95 mmHg) and reported hypertension prevalence of 1.2-4.0%. Subsequent studies report steadily increasing prevalence from 5% in 1960s to 12-15% in 1990s. Hypertension prevalence is lower in the rural Indian population, although there has been a steady increase over time here as well. . Pooling of epidemiological studies shows that hypertension is present in 25% urban and 10% rural subjects in India. At an underestimate, there are 31.5 million hypertensives in rural and 34 million in urban populations[17].

PATHOPHYSIOLOGY

The pathogenesis of essential hypertension is multifactorial and highly complex. Multiple factors modulate the blood pressure (BP) for adequate tissue perfusion and include humoral mediators, vascular reactivity, circulating blood volume, vascular caliber, blood viscosity, cardiac output, blood vessel elasticity, and neural stimulation. A possible pathogenesis of essential hypertension has been proposed in which multiple factors, including genetic predisposition, excess dietary salt intake, and adrenergic tone, may interact to produce hypertension. Although genetics appears to contribute to essential hypertension, the exact mechanism has not been established.

The natural history of essential hypertension evolves from occasional to established hypertension. After a long invariable asymptomatic period, persistent hypertension develops into complicated hypertension, in which target organ damage to the aorta and small arteries, heart, kidneys, retina, and central nervous system is evident. The progression begins with prehypertension in persons aged 10-30 years (by increased cardiac output) to early hypertension in persons aged 20-40 years (in which increased peripheral resistance is prominent) to established hypertension in persons aged 30-50 years, and, finally, to complicated hypertension in persons aged 40-60 years. One mechanism of hypertension has been described as high-output

hypertension. High-output hypertension results from decreased peripheral vascular resistance and concomitant cardiac stimulation by adrenergic hyperactivity and altered calcium homeostasis. A second mechanism manifests with normal or reduced cardiac output and elevated systemic vascular resistance due to increased vasoreactivity. Another mechanism is increased salt and water reabsorption by the kidney, which increases circulating blood volume[18].

ETIOLOGY

Environmental and genetic causes

Hypertension develops secondary to environmental factors, as well as to multiple genes, whose inheritance appears to be complex. Very rare secondary causes are related to single genes and include Liddle syndrome, glucocorticoid-remediable hyperaldosteronism, 11 beta-hydroxylase and 17 alpha-hydroxylase deficiencies, the syndrome of apparent mineralocorticoid excess, and pseudohypoaldosteronism type II. Primary or essential hypertension accounts for 90-95% of adult cases, and a small percentage of patients (2-10%) have a secondary cause.

Causes of secondary hypertension

- Polycystic kidney disease
- Chronic kidney disease
- Urinary tract obstruction
- Renin-producing tumor
- Liddle syndrome

Vascular causes

- Coarctation of aorta
- Vasculitis
- Collagen-vascular disease

Endogenous hormonal causes include the following:

- Primary hyperaldosteronism
- Cushing syndrome
- Pheochromocytoma
- Congenital adrenal hyperplasia

Neurogenic causes include the following:

- Brain tumor
- Bulbar poliomyelitis
- Intracranial hypertension

Other causes include the following:

- Hyperthyroidism and hypothyroidism
- Hypercalcemia
- Hyperparathyroidism
- Acromegaly
- Obstructive sleep apnea
- Pregnancy-induced hypertension[19].

CLINICAL PRESENTATION

- Chronic headaches
- Dizziness or Vertigo
- Blurry or double vision.
- Drowsiness
- Nausea
- Shortness of breath. Usually when this occurs people start to get a little concerned. Often by this time though the blood pressure has probably reached high enough levels to be dangerous as this is one of the last symptoms of hypertension you'll experience.
- Heart palpitations
- Fatigue - general tiredness
- A flushed face
- Nosebleeds
- A strong need to urinate often especially during the night
- Tinnitus[20].

DIAGNOSIS

The most precise way to measure blood pressure is to place a small tube or catheter into an artery and directly measure the pressures. Usually, a much simpler method is employed. The health care provider places a blood pressure cuff around the upper arm and inflates the cuff with air. As the cuff becomes filled with air, the pressure in the cuff increases, eventually cutting off the flow of blood through the

arteries in the arm. The health care provider slowly lets air leak out of the blood pressure cuff, causing the pressure in the cuff to gradually decrease. When the pressure in the cuff falls below the systolic blood pressure in the arteries, the provider begins to hear a characteristic thumping sound as blood starts to flow again in the arm. The blood pressure cuff continues to deflate, and when the pressure in the cuff falls below the diastolic blood pressure in the arteries, the characteristic thumping sound disappears. By listening for the beginning and termination of this sound and simultaneously watching the pressure gauge in the cuff when these events occur, the health care provider determines the systolic and diastolic blood pressure.

If the blood pressure is not measured correctly, the readings obtained may be artificially high. Several steps ensure that the measured blood pressure truly represents the patient's blood pressure:

1. Patients should sit with their arms supported at heart level.
2. Patients should not smoke or ingest caffeine for 30 minutes prior to blood pressure measurement.
3. Patients should sit down for at least 5 minutes before blood pressure is measured.
4. The bladder of the blood pressure cuff should encircle at least 80% of the arm. A large cuff should be used for patients with thick arms.
5. Two or more readings should be taken at least 2 minutes apart.

Evaluation of patients with high blood pressure consists primarily of the following:

- Focused history to collect important data including symptoms like chest pain
- Family history of high blood pressure
- Medical history of co-existing conditions like diabetes
- Physical examination
- Blood tests
- Electrocardiogram
- Echocardiogram or ultrasound of the heart[21].

LIFE STYLE MODIFICATION

Lifestyle modifications that effectively lower blood pressure are increased physical activity, weight loss, limited alcohol consumption, reduced sodium intake and the dietary Approaches to Stop hypertension diet. Lifestyle modification is recommended as initial therapy in stage 1 hypertension before initiation of drug therapy and as an adjunct to medication in persons already on drug therapy. In pre-hypertensives, it can reduce the incidence of hypertension and lower end-organ damage. It is emphasized that simple advice from physicians can have a positive influence on patients' motivation to make lifestyle changes[22].

DRUG THERAPY

General Therapeutic Principles

In most hypertensives there is little to be gained from the pursuit of rapid blood pressure control. The most important therapeutic goal for the vast majority is to prescribe a combination of appropriate lifestyle modifications (weight loss, salt and alcohol restriction, and increased physical activity) plus the lowest doses of drugs that allow blood pressure normalization over the long term. The erroneous clinical perception that diastolic blood pressure is the predominant pressure mediator of clinical risk contributes to physician hesitancy to intensify treatment to normalize systolic blood pressure once diastolic blood pressure has been lowered to less than 90 mm Hg. Many antihypertensive medications have dose-related side effects. Drug acquisition costs also usually increase at higher dose levels. In certain instances, cost is a major barrier to patient compliance with prescribed drug therapies. Drug acquisition costs are but one consideration, albeit an important one, in embarking on a hypertension disease management strategy[23]**.**

Diuretics

Diuretics, commonly called “water pills,” are the oldest and least expensive class of drugs used to treat hypertension .They help the kidneys eliminate sodium and water from the body. This process decreases blood volume, so heart has less to pump with each beat, which in turn lowers blood pressure. Common side effects of these drugs include frequent urination, light headedness, fatigue, diarrhea or constipation,

muscle cramps and potassium depletion, so need potassium supplements when taking these drugs.

Thiazide diuretics-**chlorothiazide,hydrochlorothiazide,chlorthalidone.**

Loop diuretic-**Furosemide.**

Potassium sparing diuretic-**Spiranolactone**[24]**.**

Beta blockers

These drugs are effective in hypertension because they decrease the heart rate and cardiac output. Even after continued use of β-blockers, cardiac output remains lower and systemic vascular resistance higher with agents that do not have intrinsic sympathomimetic or α-blocking activity. The β-blockers also decrease renin release and are more efficacious in populations with elevated plasma renin activity, such as younger white patients. The side effects of all β-blockers include inducing or exacerbating bronchospasm in predisposed patients (eg, those with asthma and some patients with chronic obstructive pulmonary disease [COPD]),sinus node dysfunction and atrioventricular (AV) conduction depression ,precipitating or worsening clinically important left ventricular failure, nasal congestion, Raynaud's phenomenon,and central nervous system symptoms with nightmares, excitement, depression, and confusion, fatigue, lethargy, and impotence may occur.

Eg-**atenolol,propranalol,labetalol.**

ACE inhibitors

ACE inhibitors are being increasingly used as the initial medication in mild to moderate hypertension. Their primary mode of action is inhibition of the renin-angiotensin-aldosterone system, but they also inhibit bradykinin degradation, stimulate the synthesis of vasodilating prostaglandins and, sometimes, reduce sympathetic nervous system activity.Side effects are chronic dry cough,hperkalemia,dizziness,skin rashes,angioodema.

Eg-Ramipril,captopril,enlapril.

Angiotensin II receptor blockers

The final active messenger of the renin-angiotensin pathway is angiotensin II. Angiotensin II binds to AT1 receptors to cause vasoconstriction and fluid retention, both of which lead to an increase in blood pressure. The angiotensin II receptor blockers lower blood pressure by blocking the AT1 receptors**.** The ARBs do not cause cough and are only infrequently associated with skin rashes.Common side effects are renal failure,hyperkalemia, hepatotoxicity, angioneurotic edema, and neuropsychiatric symptoms.

Eg-**Losartan,telmisartan,valsartan.**

Calcium channel blockers

Calcium channel antagonists block inward movement of calcium by binding to the L-type calcium channels in the heart and in smooth muscle of the pericardial vasculature.calcium channel blockers dilate coronary arteries and peripheral arterioles,but not veins.

The most common side effects of calcium channel blockers are headache, peripheral edema bradycardia, and constipation.

Eg-**verapamil,diltiazem.**

Alpha-adrenoceptor antagonists

They block postsynaptic α-receptors, relax smooth muscle, and reduce blood pressure by lowering peripheral vascular resistance. These agents are effective as single-drug therapy in some individuals, but tachyphylaxis may appear during long-term therapy.Common side effects are dizziness,fainting,low blood pressure,sudden blood pressure changes when standing after sitting.

Eg-**Prazosin, terazosin, and doxazosin.**

Drugs with central sympatholytic action

They lower blood pressure by stimulating α-adrenergic receptors in the central nervous system, thus reducing efferent peripheral sympathetic outflow. These agents are effective as single therapy in some patients, but they are usually used as second- or third-line agents because of the high frequency of drug intolerance, including sedation, fatigue, dry mouth, postural hypotension, and impotence.

Eg-**Methyldopa, clonidine, guanabenz, and guanfacine**[25].

Arteriolar dilators

They relax vascular smooth muscle and produce peripheral vasodilation. They are usually given in combination with diuretics and β-blockers in resistant patients. Common side effects are headache, palpitations, fluid retention, hirsutism, lupus-like syndrome.

Eg-**Hydralazine and minoxidil** [26]**.**

HIGH SENSITIVITY C-REACTIVE PROTEIN:

hs-CRP has emerged as a strong, robust and independent risk factor for CVD that appears to have significant clinical utility. It is a circulating acute phase reactant named initially for its capacity to bind to the c-polysaccharide of Streptococcus pneumoniae, and is synthesized primarily by the liver in response to IL-6 and IL-1β. As a risk assessment tool, it has several good points. It is very stable with very little difference in values between fresh or frozen plasma and has a long half-life of up to 20 h.It normally circulates at very low levels, but acute inflammatory processes induce marked hepatic synthesis of hs-CRP, which can induce a 100-fold serum increase.

Evidence has shown that, even in apparently healthy subjects, there is good and consistent significant relationship between baseline hs-CRP levels and risk of future cardiovascular events such as stroke, peripheral vascular disease, sudden cardiac death and myocardial infarction. In those with existing CVD, it has been shown to predict future cardiovascular events[27]. Laboratory and experimental evidence indicate that atherosclerosis, in addition to being a disease of lipid accumulation also represents a chronic inflammatory process. Thus, researchers have hypothesized that inflammatory markers such as high-sensitivity c-reactive protein (hs-CRP) may provide an adjunctive method for global assessment of cardiovascular risk. In support of this hypothesis, several large-scale prospective epidemiological studies have shown that plasma levels of hs-CRP are a strong independent predictor of risk of future myocardial infarction, stroke, peripheral arterial disease, and vascular death among individuals without known cardiovascular disease. In addition, among patients with acute coronary ischemia, stable angina pectoris, and a history of

myocardial infarction, levels of hS-CRP have been associated with increased vascular event rates.

Based in part on these data, high-sensitivity assays for CRP have become available in standard clinical laboratories. However, clinical application of hs-CRP testing will depend not only on demonstration of independent predictive value, but also on demonstration that addition of hs-CRP testing to traditional screening methods improves cardiovascular risk prediction. Furthermore, application of hs-CRP as a tool to assist in global risk assessment requires knowledge of population distribution of hs-CRP, clinical characteristics of hs-CRP evaluation, and magnitude of risk of future coronary events that can be expected at each level of hs-CRP[28].

High Sensitivity C-Reactive Protein (hs-CRP) Assay

The high-sensitivity C-reactive protein (hs-CRP) assay is a quantitative analysis test of very low levels of C-reactive protein (CRP) in the blood. Following a systematic review of the association between inflammatory markers and coronary heart disease and stroke, the American Heart Association (AHA) and Centers for Disease Control and Prevention (CDC) developed a scientific statement that recommends hs-CRP as a more sensitive assay for the prediction of vascular disease, compared to traditional assays for circulating C-reactive protein levels[29] .

The AHA/CDC Scientific Statement Summary

- hs-CRP is a global indicator of future vascular events in adults without any previous history of cardiovascular disease.
- hs-CRP enhances risk assessment and therapeutic outcomes in primary CVD prevention.
- hs-CRP acts as an independent marker for evaluating the possibility of recurrent cardiac events such as myocardial infarction or restenosis, after percutaneous coronary intervention.

Clinical Applications

hs-CRP in Atherosclerosis and Plaque Instability/Inflammation

With the recognition of the crucial link between arterial damage, inflammatory processes, and coronary atherosclerosis, hs-CRP estimation has assumed a vital role

in cardiac risk assessment. C-reactive protein is an important pathogenic factor for atherosclerosis and induces several reactions involved in atherothrombogenesis:

- Activates complement and attacks monocytes.
- Incites endothelial dysfunction.
- Augments a procoagulant state.
- Contributes to plaque instability/rupture.

hs-CRP in Risk Stratification and Risk Assessment

hs-CRP levels help in cardiac risk stratification and assessment, and it are a key prognostic factor in conditions such as:

- Acute coronary syndrome.
- Stroke.
- Peripheral artery disease.
- Post-MI complications such as cardiac failure.

Risk Stratification

hs-CRP is used to determine the probability of recurrence of cardiac events in patients with stable coronary heart disease and ACS.

Risk Assessment

The hs-CRP assay has been recommended in patients with intermediate risk of coronary heart disease in order to determine the need for further evaluation and therapy[30].

DRUG PROFILE

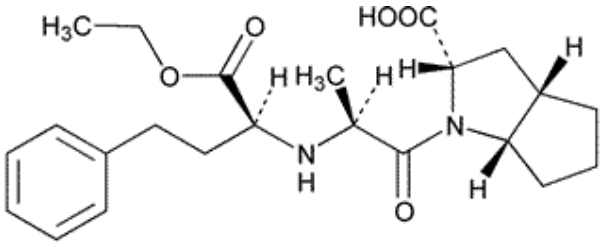
RAMIPRIL

BRAND NAME: Cardace, Macpril ,Ramace

CHEMICAL NAME: [2S - [1[R*(R*)],2α,3aβ,6aβ]] - 1 - [2 - [[1 - (Ethoxycarbonyl) - 3 - phenylpropyl]amino] - 1 - oxopropy l]octahydrocylopenta[b]pyrrole-2-carboxylic acid.

CHEMICAL FORMULA: $C_{21}H_{28}N_2O_{51}$

STRUCTURAL FORMULA:



DESCRIPTION:

Ramipril is a prodrug belonging to the angiotensin-converting enzyme (ACE) inhibitor class of medications. It is metabolized to ramiprilat in the liver and to a lesser extent, kidneys. Ramiprilat is a potent, competitive inhibitor of ACE, the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII). ATII regulates blood pressure and is a key component of the renin-angiotensin-aldosterone system (RAAS). Ramipril may be used in the treatment of hypertension, congestive heart failure, nephropathy, and to reduce the rate of death, myocardial infarction and stroke in individuals at high risk of cardiovascular events[31].

DOSAGE FORM: Tablet

MECHANISM OF ACTION:

There are two isoforms of ACE: the somatic isoform, which exists as a glycoprotein comprised of a single polypeptide chain of 1277; and the testicular

isoform, which has a lower molecular mass and is thought to play a role in sperm maturation and binding of sperm to the oviduct epithelium. Somatic ACE has two functionally active domains, N and C, which arise from tandem gene duplication. Although the two domains have high sequence similarity, they play distinct physiological roles. The C-domain is predominantly involved in blood pressure regulation while the N-domain plays a role in hematopoietic stem cell differentiation and proliferation. ACE inhibitors bind to and inhibit the activity of both domains, but have much greater affinity for and inhibitory activity against the C-domain. Ramiprilat, the principle active metabolite of ramipril, competes with ATI for binding to ACE and inhibits and enzymatic proteolysis of ATI to ATII. Decreasing ATII levels in the body decreases blood pressure by inhibiting the pressor effects of ATII .Ramipril also causes an increase in plasma renin activity likely due to a loss of feedback inhibition mediated by ATII on the release of renin and/or stimulation of reflex mechanisms via baroreceptors[32].

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS:

It is an inactive prodrug that is converted to ramiprilat in the liver, the main site of activation, and kidneys. Ramiprilat confers blood pressure lowing effects by antagonizing the effect of the RAAS. The RAAS is a homeostatic mechanism for regulating hemodynamics, water and electrolyte balance. During sympathetic stimulation or when renal blood pressure or blood flow is reduced, renin is released from the granular cells of the juxtaglomerular apparatus in the kidneys. In the blood stream, renin cleaves circulating angiotensinogen to ATI, which is subsequently cleaved to ATII by ACE. ATII increases blood pressure using a number of mechanisms. First, it stimulates the secretion of aldosterone from the adrenal cortex. Aldosterone travels to the distal convoluted tubule (DCT) and collecting tubule of nephrons where it increases sodium and water reabsorption by increasing the number of sodium channels and sodium-potassium ATPases on cell membranes. Second, ATII stimulates the secretion of vasopressin (also known as antidiuretic hormone or ADH) from the posterior pituitary gland. ADH stimulates further water reabsorption from the kidneys via insertion of aquaporin-2 channels on the apical surface of cells of the

DCT and collecting tubules. Third, ATII increases blood pressure through direct arterial vasoconstriction. Stimulation of the Type 1 ATII receptor on vascular smooth muscle cells leads to a cascade of events resulting in myocyte contraction and vasoconstriction. In addition to these major effects, ATII induces the thirst response via stimulation of hypothalamic neurons. ACE inhibitors inhibit the rapid conversion of ATI to ATII and antagonize RAAS-induced increases in blood pressure. ACE (also known as kininase II) is also involved in the enzymatic deactivation of bradykinin, a vasodilator. Inhibiting the deactivation of bradykinin increases bradykinin levels and may sustain the effects of ramiprilat by causing increased vasodilation and decreased blood pressure.

PHARMACOKINETICS:

Absorption

Bioavailability

Following oral administration, peak plasma concentrations of ramipril usually attained within 1 hour. Peak plasma concentrations of ramiprilat attained within 2–4 hours after oral dose. About ≥50–60% of an oral dose is absorbed.

Following multiple oral doses (≥2 mg), >90% inhibition of plasma ACE activity achieved 4 hours after dosing.

Following multiple oral doses (≥2 mg), inhibition of >80% of plasma ACE activity persists for about 24 hours.

Food decreases rate but not extent of absorption.

Distribution

Distributes into a large peripheral compartment. Crosses the placenta. Undetectable in human milk following single oral dose; not known whether distributed into milk following multiple doses.

Plasma Protein Binding

Ramipril: About 73%.

Ramiprilat: About 56%.

Metabolism

Metabolized mainly in the liver, principally to an active metabolite, ramiprilat.

Elimination Route

Excreted in urine (60%) as unchanged drug and ramiprilat and in feces (approximately 40%).

Half-life

Triphasic; apparent elimination half-life of ramiprilat: Approximately 13–17 hours**.**

OVER DOSAGE

May lead to severe hypotension. Normal saline infusion may be used for treatment. Overdose symptoms may include feeling extremely dizzy or light-headed, or fainting, excessive peripheral vasodilation with marked hypotension and shock, bradycardia, electrolyte disturbances, and renal failure.

ROUTE OF ADMINISTRATION: oral.

DOSAGE FORM/STRENGTH: 1**.**25 mg, 2.5mg, 5 MG,10mg.

INDICATIONS:

For the management of mild to severe hypertension. May be used to reduce cardiovascular mortality following myocardial infarction in hemodynamically stable individuals who develop clinical signs of congestive heart failure within a few days following myocardial infarction. To reduce the rate of death, myocardial infarction and stroke in individuals at high risk of cardiovascular events. May be used to slow the progression of renal disease in individuals with hypertension, diabetes mellitus and microalbuminuria or overt nephropathy.

CONTRAINDICATIONS:

Intestinal Angioedema, Head and Neck Angioedema, Method of Removing Waste/Poison from Blood with Dialysis, Renal Artery Stenosis, Liver Problems, Kidney Disease, Systemic Lupus Erythematosus, Scleroderma, Disorder of the Connective Tissue, Severe Vomiting, Severe Diarrhea, Kidney Problems Causing a Decreased Amount of Urine to be Passed, Azotemia, Abnormal Liver Function Tests,

Allergy Shots, Pregnancy, Low Amount of Sodium in the Blood, Extreme Loss of Body Water, High Amount of Potassium in the Blood, Inherited Disorder of Continuing Episodes of Swelling, Decreased Neutrophils a Type of White Blood Cell.

WARNINGS:

When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, ramipril should be discontinued as soon as possible. Ramipril should be used with caution in: the elderly (particularly those taking diuretics or with heart failure, kidney or liver problems), those with poor liver or kidney function, patients taking diuretics, those who are dehydrated or on a low-salt diet, those undergoing dialysis or a form of blood treatment called apheresis, and children.

PRECAUTIONS:

Pregnancy

Category D (second, third trimester); Category C (first trimester). Discontinue use in pregnant patients; fetal/neonatal injury and death have occurred. Closely observe infants with histories of in utero exposure.

Hyperkalemia

Possible hyperkalemia, especially in patients with renal impairment or diabetes mellitus and those receiving drugs that can increase serum potassium concentration (e.g., potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes).

Cough

Persistent and nonproductive cough; resolves after drug discontinuance.

Renal Impairment

Systemic exposure to ramiprilat may be increased. Initial dosage adjustment may be necessary depending on degree of renal impairment[33].

ADVERSE DRUG REACTIONS:

Nausea, vomiting, diarrhea, dizziness, fatigue, head ache, abdominal pain, cough, angioneuritic odema of face, lips, tongue, glottis and larynx, syncope, renal

impairment, hyper sensitivity reactions, severe hypotension and angioedema. Rarely symptomatic hypertension may occur.

DRUG-DRUG INTERACTIONS:

Angiotensin receptor blockers

Combining ACE inhibitors (such as ramipril) with ARBs may increase the risk of various problems (such as kidney damage, high potassium levels, or dangerously low blood pressure) without providing significant benefit. In general, ramipril should not be combined with ARB medications.

Diuretics

If taking ramipril with a diuretic, blood pressure may decrease too much. The risk of this happening can be reduced by either stopping the diuretic (under a healthcare provider's supervision) or increasing salt intake prior to starting the ramipril.

Injectable Gold

Reactions have been reported in people taking ramipril who received gold injections. These reactions included symptoms such as facial flushing, nausea, vomiting, and low blood pressure.

Lithium

Ramipril may increase the risk of lithium toxicity and may increase the lithium levels in the blood. Blood lithium levels should be monitored to adjust the dose.

Nonsteroidal Anti-Inflammatory Drugs

Ramipril can interact with NSAIDS in several ways. The combination could cause blood pressure to increase or may cause swelling (edema), especially if have congestive heart failure (CHF). If elderly, have kidney disease or kidney failure, or are taking a diuretic or are dehydrated, taking NSAIDs and ramipril together may cause kidney failure.

Potassium

If taking a potassium product together with ramipril, the levels of potassium in blood may become too high. This can cause serious problems.

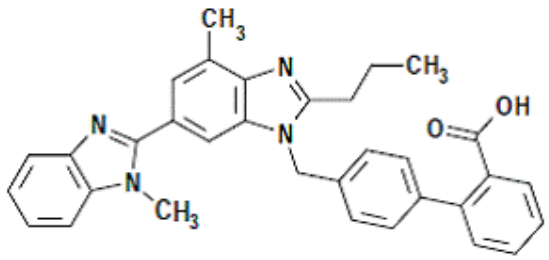
TELMISARTAN

BRAND NAME: TELMA, CREZAR, TAZLOC.

CHEMICAL NAME: 4'-[(1,4'-dimethyl-2'-propyl [2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid.

CHEMICAL FORMULA: $C_{33}H_{30}N_4O_2$

STRUCTURAL FORMULA:



DESCRIPTION:

Telmisartan is a white to slightly yellowish solid. It is practically insoluble in water and in the pH range of 3 to 9, sparingly soluble in strong acid (except insoluble in hydrochloric acid), and soluble in strong base.

DOSAGE FORM: Tablet

MECHANISM OF ACTION:

Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT_1-receptor by binding reversibly and selectively to the receptors in vascular smooth muscle and the adrenal gland. As angiotensin II is a vasoconstrictor, which also stimulates the synthesis and release of aldosterone, blockage of its effects results in decreases in systemic vascular

resistance. Telmisartan does not inhibit the angiotensin converting enzyme, other hormone receptors, or ion channels. Studies also suggest that telmisartan is a partial agonist of PPARγ, which is an established target for antidiabetic drugs. This suggests that telmisartan can improve carbohydrate and lipid metabolism, as well as control insulin resistance without causing the side effects that are associated with full PPARγ activators[34].

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS:

Telmisartan is an orally active nonpeptide angiotensin II antagonist that acts on the AT_1 receptor subtype. It has the highest affinity for the AT_1 receptor among commercially available ARBS and has minimal affinity for the AT_2 receptor. New studies suggest that telmisartan may also have PPARγ agonistic properties that could potentially confer beneficial metabolic effects, as PPARγ is a nuclear receptor that regulates specific gene transcription, and whose target genes are involved in the regulation of glucose and lipid metabolism, as well as anti-inflammatory responses. This observation is currently being explored in clinical trials. Angiotensin II is formed from angiotensin I in a reaction catalyzed by angiotensin-converting enzyme (ACE, kininase II). Angiotensin II is the principal pressor agent of the renin-angiotensin system, with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium. Telmisartan works by blocking the vasoconstrictor and aldosterone secretory effects of angiotensin II.

PHARMACOKINETICS:

Absorption

Bioavailability

Absolute bioavailability is dose dependent: 42% at 40 mg, 58% at 160 mg. Peak plasma concentration generally reached at 0.5–1 hour following oral administration. Antihypertensive effect evident within 2 weeks, with maximum BP reduction after 4 weeks[35].Food slightly reduces bioavailability. In patients with

hepatic insufficiency, plasma telmisartan concentrations are increased and absolute bioavailability approaches 100%.

Distribution

Crosses the placenta and is distributed in the fetus in animals.
Distributed into milk in rats; not known whether distributed into human milk.
Plasma Protein Binding.
>99.5% (principally albumin and α_1-acid glycoprotein).

Metabolism

Metabolized in liver (via conjugation) to inactive metabolite.
Not metabolized by CYP isoenzymes.

Elimination Route

Eliminated mainly (>97%) as unchanged drug in feces (via bile); small amounts (<1%) eliminated in urine.

Half-life

Biphasic; terminal half-life is approximately 24 hours.

OVER DOSAGE:

Overdose symptoms may include fast or slow heartbeat, dizziness. The most likely manifestations of overdosage with telmisartan would be hypotension, dizziness and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation.

DOSAGE FORM/STRENGTH: 20 mg , 40 mg ,80 mg

INDICATIONS:

Used alone or in combination with other classes of antihypertensives for the treatment of hypertension. Also used in the treatment of diabetic nephropathy in

hypertensive patients with type 2 diabetes mellitus, as well as the treatment of congestive heart failure (only in patients who cannot tolerate ACE inhibitors).

CONTRAINDICATIONS:

Renal Artery Stenosis, Abnormally Low Blood Pressure, Liver Problems, Blockage of a Bile Duct, Kidney Disease, Pregnancy, Decreased Blood Volume, Extreme Loss of Body Water, High Amount of Potassium in the Blood.

WARNINGS:

When used in pregnancy, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, ramipril should be discontinued as soon as possible. If oligohydramnios is observed, ramipril tablets should be discontinued unless they are considered life-saving for the mother. Infants with histories of in utero exposure to an angiotensin II receptor antagonist should be closely observed for hypotension, oliguria, and hyperkalemia.

PRECAUTIONS:

Telmisartan may cause extreme low blood pressure in some people. Extreme low blood pressure is more likely to happen in people who are taking a diuretic, are on dialysis, or have congestive heart failure.

Telmisartan is a pregnancy Category C medicine for the first trimester and a pregnancy Category D medicine for the second and third trimesters, meaning that it poses potential health risks to your unborn child.

While taking telmisartan, do not use potassium supplements or salt substitutes with potassium unless you have discussed this with your doctor.

This medication may cause a decrease in kidney function, especially in people who are elderly, have kidney disease, have severe congestive heart failure (CHF), or are taking nonsteroidal anti-inflammatory drugs (NSAIDs) or diuretics (water pills).

ADVERSE DRUG REACTIONS:

Severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue; unusual hoarseness); change in the amount of urine produced or painful urination; chest pain; difficulty swallowing; fast, slow, or irregular heartbeat; fever, chills, or persistent sore throat; increased or excessive sweating; muscle pain or cramps; severe or persistent vomiting or diarrhea; severe or persistent weakness; shortness of breath; swelling of the arms or legs; symptoms of low blood pressure (eg, fainting, lightheadedness, severe dizziness); tendon or joint pain[36].

DRUG-DRUG INTERACTIONS:

With telmisartan, drugs such as potassium supplements or potassium-sparing diuretics may cause an interaction. Not only can drug interactions with telmisartan cause body to metabolize the medicines differently than intended, but they may also result in side effects such as extremely low blood pressure or excessive drug levels in your blood.

Concurrent use increases digoxin concentration; increases risk of lithium toxicity; increases risk of hyperkalaemia with potassium sparing diuretics, heparin[37].

LITERATURE REVIEW

1. **Italo Proto**[38]**et al.** compared the effects of ramipril and telmisratan on high sensitivity c-reactive protein and endothelial progenitor cells after acute coronary syndrome.42 patients with ACS were randomized after successful percutaneous coronary intervention to ramipril 5 mg/day (22 patients) or telmisartan 80 mg/day (20 patients). Peripheral blood samples were drawn at baseline and at 20 days to measure high-sensitivity C-reactive protein and to assess 4 populations of progenitor cells by flow cytometry, namely CD34+/KDR+, CD34+/CD133+ CD34+/CD133+/CD45-, and CD34+/KDR+/CD45- cells CD34+/KDR+/CD45- cells. High-sensitivity C-reactive protein levels, similar in the 2 groups at baseline, were significantly more decreased by telmisartan than by ramipril at follow up ($p = 0.013$ for time-by-drug interaction). The main effect for time was also significant ($p < 0.001$). CD34+/KDR+ and CD34+/CD133+ cells were similar at baseline and did not change over time ($p = 0.2$ and $p = 0.1$, respectively). In contrast, for CD34+/KDR+/CD45- and CD34+/CD133+/CD45- cells, a significant increase with time was seen ($p = 0.02$ and $p = 0.002$, respectively) and no differential effect of either drug was seen. In conclusion, telmisartan shows a more potent anti-inflammatory effect than ramipril after an ACS. The 2 drugs do not show a differential effect on endothelial progenitor cell mobilization.

2. **Myung Ho Jeong** [39] **et al.** studied relation between High-Sensitivity C-Reactive Protein and Coronary Plaque Components in Patients With Acute Coronary Syndrome. Virtual histology-intravascular ultrasound (VH-IVUS) is used to evaluate the relationship between high-sensitivity C-reactive protein levels and plaque components in 279 acute coronary syndrome patients.Patients are divided into three groups according to their hs-CRP levels {lowest tertile <0.07 mg/dL (n=93), middle tertile ≥0.07, <0.4 mg/dL (n=93), and highest tertile ≥0.4 mg/dL (n=93)}. Thin-cap fibroatheroma (TCFA) was defined as focal, necrotic core (NC)-rich (≥10% of the cross-sectional area) plaques in

contact with the lumen in a plaque burden ≥40%.The highest tertile group was mostly diabetics (20%, 27%, 40%, p=0.009), and had the greatest plaque plus media volume (163±139/mm^3 vs. 201±155/mm^3 vs. 232±176/mm^3, p=0.013). The highest tertile group had the greatest absolute and % NC volumes (13.6±15.1 mm^3 vs. 14.8±14.2 mm^3 vs. 23.7±24.3 mm^3, p<0.001, and 14.9±8.7% vs. 16.0±8.7% vs. 19.5±10.2%, p=0.024, respectively). The culprit lesion TCFA was observed most frequently in the highest tertile group (28% vs. 35% vs. 55%, p=0.006). By multivariable analysis, absolute NC volume was an independent predictor of hs-CRP elevation {odds ratio (OR); 1.03, 95% confidence interval (CI)=1.06-1.21, p=0.004}, and hs-CRP was an independent predictor of TCFA (OR; 1.86, 95% CI=1.11-2.90, p=0.010).VH-IVUS analysis has demonstrated that ACS patients with elevated hs-CRP have more vulnerable plaque component compared with ACS patients with normal hs-CRP.

3. **Deborah B Diercks [40]et al.** compared the Value of high-sensitivity C-reactive protein in low risk chest pain observation unit patients. A total of 958 patients had hs-CRP testing as part of their CPEU evaluation. Excluded from the analysis were 39 patients lost to follow-up. The final cohort comprised 478 (52%) women and 441 (48%) men with a median age of 56 (IQR 48-64). ACS was diagnosed in 128 (13.4%). The median cohort hs-CRP value was 2.2 mg/l (IQR 0.7, 5.8) and 2.3 mg/l (IQR 0.6, 5.9) in those with and without ACS, respectively. In the multivariate analysis hs-CRP was not independently associated with the diagnosis of ACS (0.99; 95% CI 0.98 - 1.01). In large patient cohort managed in a single-center CPU, measurement of hs-CRP did not enhance the diagnostic accuracy for ACS. Routine hs-CRP as a diagnostic tool should not be recommended in the CPU setting.

4. **Riedel M[41]et al.** suggested that High-sensitivity C-reactive protein has been reported to have a prognostic value immediately after acute coronary syndrome and to be associated with the onset of cardiovascular events in patients with stable and unstable angina pectoris. Aim is to evaluate whether or not hsCRP levels can be used to predict future CV events in a prospective study of post-

ACS patients receiving an optimized medical treatment (OMT) secondary-prevention regimen. Methods: OMT along with therapeutic and dietary education programmes were started during the acute phase, then monitored and adjusted as needed at 3 months post ACS. hsCRP was measured at 3 months after the ACS, and a global evaluation of atherosclerosis burden and risk factors were also evaluated at this time point. The study population was divided into tertiles based on their hsCRP value and followed for CV events. Results: A total of 1202 consecutive patients with hsCRP <15 mg/l were included in the study, 795 of which were followed for an average of 22 months. LDL-cholesterol, HbA(1c), waist circumference, systolic blood pressure, metabolic syndrome, tobacco consumption, and atherosclerosis burden were higher in patients in the second and third tertile of hsCRP ($p < 0.001$) than those in the first tertile, at 3 months. hsCRP level was not found to be associated with recurrence of total CV events in univariate analysis. We further examined the effect of adding hsCRP levels to the Framingham risk evaluation score, and found no significant improvement the C-statistics of the Framingham risk evaluation score. Conclusion: hsCRP is associated with CV risk factors, but is not an independent predictor of future events in post-ACS patients receiving an OMT secondary-prevention regimen.

5. **Puri VK[42]et al.** suggested that Percutaneous coronary intervention provokes an inflammatory reaction, as shown by increased concentrations of plasma C-reactive protein after PCI. However, the changes of CRP levels after PCI in patients with acute coronary syndrome have not been well evaluated. They evaluated the characteristics of the patients with elevated CRP response after PCI and whether an increase in CRP after PCI predicts long-term prognosis in patients with ACS. We studied consecutive 360 patients with ACS who underwent elective coronary stenting. Inflammatory response to PCI was calculated as the difference between the peak postprocedural hsCRP level and the preprocedural hsCRP level (ΔCRP). Twelve months follow-up data were obtained and clinical outcomes were compared with ΔCRP. In receiver

operating characteristics analyses, the cutoff point of ΔCRP for major adverse cardiac events was 3.0 mg/l, which yielded sensitivity of 61.7% and specificity of 69.7%. The patients with ΔCRP > 3 mg/l revealed higher incidence of myocardial infarction (37.7 vs 14.6%, $P < 0.001$), and ACC/AHA type B2/C lesion (81.5 vs 68.7%, $P = 0.006$) than in patients with low ΔCRP. White blood cell count, low-density lipoprotein cholesterol, peak creatinine kinase-MB, and peak troponin T were significantly elevated in patients with ΔCRP > 3 mg/l than in those with ≤3 mg/l. There was significant correlation between ΔCRP and the changes in troponin T after PCI ($r = 0.210$, $P < 0.001$). An increase in hsCRP > 3 mg/l after PCI had a higher predictive value for the occurrence of MACE than low hsCRP elevation (hazard ratio 2.1, $P = 0.005$). In multivariate analysis, ΔCRP and peak troponin T were independent predictors of MACE ($P < 0.001$ and $P = 0.013$, respectively). In conclusion, postprocedural hsCRP elevation >3 mg/l was associated with higher incidence of MACE in patients with ACS. ΔCRP determinations may be of value for risk stratification after PCI.

6. **Sethi R**[43] **et al.** demonstrated correlation between high sensitivity C-reactive protein and socio-economic class in patients of acute coronary syndrome.Mean levels of hs-CRP in lower, middle and upper SES were 2.3 +/- 2.1 mg/L, 0.8 +/- 1.7 mg/L and 1.2 +/- 1.5 mg/L, respectively. hs-CRP levels were significantly higher in low SES compared with both upper SES (p = 0.033) and middle SES (p = 0.001). Prevalence of more than one traditional CAD risk factors was seen in 13.5%, 37.5% and 67.67 percent; in patient of lower, middle and upper SES. It was observed that multiple risk factors had a linear correlation with increasing SES. Of the four traditional risk factors of CAD, smoking was the only factor which was significantly higher in lower SES (73%) as compared to middle (51.67 percent;) and upper (39.4%) SES. We found that 62.3%, 20.8% and 26.5% patients of low, middle and upper SES had hs-CRP values in the highest tertile. Median value of the Framingham risk score in low, middle and upper SES as 11, 14 and 18, respectively. We

observed that at each category of Framingham risk, low SES had higher hs-CRP.Conclusion from the study is that patient of lower SES have significantly higher levels of hs-CRP despite the fact that they have lesser traditional risk factors and lower Framingham risk. These findings add credit to our belief that inflammation may be an important link in the pathophysiology of atherosclerosis and its complications especially in patients of low SES who do not have traditional risk factors.

7. **Torres JL**[44] **et al.** studied the importance of High sensitivity C-reactive protein in clinical practice.As a growing number of patients with low low-density lipoprotein cholesterol levels are diagnosed with atherosclerosis, research has shifted toward markers of inflammation in an attempt to improve global cardiovascular risk prediction. These markers include cytokines, cell adhesion molecules, and acute phase reactants like high sensitivity C-reactive protein, an innate immune response protein. When measured with new high-sensitivity assays, levels of high sensitivity C-reactive protein have proven to predict future cardiovascular risk at all levels of low-density lipoprotein cholesterol, at all levels of the Framingham Risk Score, and at all levels of the metabolic syndrome. Among apparently healthy men and women, levels of high sensitivity C-reactive protein of <1, 1-3, and >3 mg/L distinguish between those at low, moderate, and high risk for future cardiovascular disease, respectively. In clinical practice, high sensitivity C-reactive protein should be used along with lipid evaluation as part of global risk assessment. Improved knowledge of cardiovascular risk should lead to improved compliance with both lifestyle and pharmacologic interventions designed to prevent future cardiovascular events.

8. **Hannes F**[45] **et al.** studied the role of inflammation in the pathophysiology of acute coronary syndromes. All stages of atherosclerotic plaques are characterized by an inflammatory component, in which T lymphocytes and macrophages orchestrate lesion progression and destabilization by releasing

cytokines (e.g., interferon-gamma, tumor necrosis factor-alpha, tissue factor). At the extreme end of this process plaque rupture occurs, which may manifest clinically as an acute coronary syndrome. Hence, measuring this atherosclerosis-inherent inflammation may help predicting cardiovascular events. Accordingly, different soluble inflammatory markers were studied for their predictive value in acute coronary syndromes. Special attention was paid to high-sensitivity C-reactive protein (hs-CRP) and soluble CD40 ligand (sCD40L). The latter seems not only to be a marker of inflammation and platelet activation, but is suggested to directly destabilize atherosclerotic plaques by stimulating pro-inflammatory T lymphocytes. Therefore, reduction of soluble inflammatory markers is an attractive target for future therapeutic strategies. Statins and glycoprotein IIb/IIIa antagonists, well-established treatments in acute coronary syndromes, were demonstrated to decrease hs-CRP and sCD40L. Whether this reduction translates into a better prognosis has to be investigated in further studies.

9. **Shishehbor MH**[46] **et al** proved that Inflammation plays a pivotal role in all stages of atherogenesis, from foam cell to plaque formation to rupture and ultimately to thrombosis. Insight gained from recent basic and clinical data linking inflammation to atherosclerosis has yielded important diagnostic and prognostic information. Low-grade chronic inflammation as measured by high sensitivity C-reactive protein predicts future risk of acute coronary syndrome independent of traditional cardiovascular risk factors. In addition, individuals with higher "inflammatory burden" gain the largest absolute risk reduction with aggressive risk-lowering therapy. The link between inflammation and atherosclerosis provides a new venue for future pharmacologic agents that may slow the progression of atherosclerosis by inhibiting inflammation.

10. **Matsumoto D**[47]**et al.** suggested that Elevated circulating C-reactive protein is commonly observed in patients with acute coronary syndrome suggesting

enhanced inflammation in vulnerable plaques. However, few data are available on the relationship between the levels of CRP and the histological composition of coronary plaque. They investigated the relationship between plasma high sensitive CRP level and coronary plaque component with Virtual Histology intravascular ultrasound (VH-IVUS).IVUS spectral analysis revealed that elevated plasma high sensitve CRP level was correlated with necrotic core volume in patients with ACS, both in culprit and non-culprit lesions, suggesting enhanced vascular inflammation.

11. **White CM[48]et al.** suggested that Standard therapies for the management of stable ischemic heart disease partially reduce the risk of a future acute coronary syndrome. Among patients with chronic heart failure or previous myocardial infarction and left ventricular dysfunction, a large body of evidence supports the benefits of angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers and, in heart failure, combined therapy with these agents. In contrast, there is less certainty regarding outcomes of ACE inhibitors and ARBs for people with stable IHD who have preserved left ventricular function and no signs or symptoms of heart failure.

12. **Ram C[49]et al.** proposed that Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers have shown cardioprotective and renoprotective properties. These agents are recommended as first-line therapy for the treatment of hypertension and the reduction of cardiovascular risk. Early studies pointed to the cardioprotective and renoprotective effects of ARBs in high-risk patients. The ongoing Telmisartan Alone and in combination with ramipril global endpoint Trial (ONTARGET) established the clinical equivalence of the cardioprotective and renoprotective effects of telmisartan and ramipril, but did not find an added benefit of the combination over ramipril alone. Similar findings were observed in the Telmisartan Randomized Assessment Study in ACE Intolerant subjects with cardiovascular Disease (TRANSCEND) trial conducted in ACEI-intolerant patients. In ONTARGET, telmisartan had a better tolerability profile with similar renoprotective properties compared with ramipril, suggesting a potential clinical benefit over

ramipril. The recently completed Olmesartan reducing Incidence of endstage renal disease in diabetic nephropathy Trial (ORIENT) and Olmesartan and Calcium Antagonists Randomized (OSCAR) studies will further define the role of ARBs in cardioprotection and renoprotection for high-risk patients.

13. **Frampton JE[50] et al.**suggested that Telmisartan a well established angiotensin type 1 receptor antagonist, is indicated in the EU for the reduction of cardiovascular morbidity in patients with manifest atherothrombotic cardiovascular disease or type 2 diabetes mellitus with documented target organ damage, as well as for the treatment of hypertension. In the pivotal ONTARGET trial, which enrolled ACE inhibitor-tolerant patients at high vascular risk, telmisartan 80 mg once daily added to existing, proven therapy was noninferior to ramipril 10 mg once in terms of CVD prevention. Moreover, telmisartan was better tolerated than ramipril, as reflected in, for example, lower incidences of permanent treatment discontinuations due to cough and angioedema. The placebo-controlled TRANSCEND and PROFESS studies provided supporting evidence for the effectiveness of telmisartan in preventing cardiovascular events, although the drug appeared to have neither a beneficial nor a harmful impact on cardiovascular mortality. The TRANSCEND trial also demonstrated that telmisartan was well tolerated in ACE inhibitor-intolerant patients at high vascular risk. On the basis of these findings, telmisartan can be considered as an effective treatment option for CVD prevention in patients at high vascular risk. Consideration may be given to prescribing the drug as an alternative to ramipril in patients who are able to tolerate ACE inhibitors and potentially instead of ramipril in patients who are unable to tolerate ACE inhibitors.

14. **Domenico Galzerano[51]et al.** suggested that Blockade of the renin–angiotensin system is an important approach in managing high blood pressure and has increasingly been shown to affect cardiovascular disease processes mediated by

angiotensin II throughout the cardiovascular and renal continua. Telmisartan is an angiotensin II receptor blocker displaying unique pharmacologic properties including a longer half life than any other ARB that result in large and sustained reductions of blood pressure. In patients with mild-to-moderate hypertension, telmisartan has proved superior to other antihypertensive agents (valsartan, losartan, ramipril, perindopril, and atenolol) in controlling blood pressure particularly towards the end of the dosing interval. There is also clinical evidence that telmisartan reduces left ventricular hypertrophy, reduces arterial stiffness and the recurrence of atrial fibrillation, and confers renoprotection. The ongoing Telmisartan alone and in combination with Ramipril global endpoint trial (ONTARGET®) study has demonstrated that telmisartan has similar cardiovascular protective effects to ramipril in a large, high-risk patient population but was better tolerated. The powerful and sustained blood pressure control apparent in clinical trials, together with cardiovascular protection and tolerability demonstrated in ONTARGET® means that telmisartan may be a preferred option for patients with hypertension.

15. **Ramón C[52] et al.** proposed that Clinical studies have demonstrated a different effect on blood pressure of some angiotensin-converting enzyme inhibitors when administered in the morning versus the evening. Their administration at bedtime resulted in a higher effect on nighttime blood pressure as compared with morning dosing. This study investigated the administration time-dependent effects of ramipril on ambulatory blood pressure. They studied 115 untreated hypertensive patients, 46.7±11.2 years of age, randomly assigned to receive ramipril (5 mg/d) as a monotherapy either on awakening or at bedtime. Blood pressure was measured for 48 hours before and after 6 weeks of treatment. The blood pressure reduction during diurnal activity was similar for both treatment times. Bedtime administration of ramipril, however, was significantly more efficient than morning administration in reducing asleep blood pressure. The awake:asleep blood pressure ratio was decreased after

ramipril on awakening but significantly increased toward a more dipping pattern after bedtime dosing. The proportion of patients with controlled ambulatory blood pressure increased from 43% to 65% (*P*=0.019) with bedtime treatment. Nocturnal blood pressure regulation is significantly better achieved at bedtime as compared with morning administration of ramipril, without any loss in efficacy during diurnal active hours. This might be clinically important, because nighttime blood pressure has been shown to be a more relevant marker of cardiovascular risk than diurnal mean values. The change in the dose-response curve, increased proportion of controlled patients, and improved efficacy on nighttime blood pressure with administration of ramipril at bedtime should be taken into account when prescribing this angiotensin-converting enzyme inhibitor for treatment of essential hypertension.

16. **Paweł Petkow-Dimitrow[53]et al.** suggested that Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers posses multiple beneficial effects such as cardioprotection, cerebroprotection, nephroprotection which provide opportunity to select the most suitable drug for the target vascular bed (e.g. coronary, or cerebral circulation). In some clinical settings, combined therapy ACE-I with ARB (double blockage of the renin-angiotensin- -aldosteron system) may appear the most effective. These drugs (especially ARB) may successfully prevent atrial fibrillation and play a protective role in metabolic syndrome. Recently, it has been demonstrated that losartan is able to inhibit vasodilatation of the aorta in marfan syndrome, which might prevent sudden death due to aorta rupture. An increasing role of ARB is most beneficial in hipotensive therapy (inhibition/regression of hypertension-related organ damage). With particular interest, results of the ONTARGET study are being awaited. This study is focused on the effect of double blockage (ramipril and telmisartan) on reduction of the occurrence of myocardial infarction, stroke, and heart failure.

17. **Philippe Gosse**[54] **et al**. made a review that measurement of blood pressure in the clinic may provide a false impression of blood pressure control. Ambulatory blood pressure monitoring (ABPM) allows the automatic recording of the circadian variation in blood pressure and evaluation of the efficacy of antihypertensive medication throughout the dosing interval. Ambulatory blood pressure provides more effective prediction of cardiovascular risk; blood pressure control at the time of heightened risk in the early morning after walking and before taking the next dose of medication is becoming important in order to improve long-term prognosis. To achieve blood pressure control in the early morning, a long-acting antihypertensive agent is essential. Telmisartan, an angiotensin II receptor blocker, as well as having a terminal elimination halflife of 24 h, has a large volume of distribution due to its high lipophilicity. The efficacy of telmisartan 80 mg monotherapy has been demonstrated using ABPM, with superior reduction in mean values for the last 6 h of the dosing interval compared with ramipril 10 mg and valsartan 80 mg. In addition, telmisartan 80 mg provides superior blood pressure control after a missed dose compared with valsartan 160. When combined with hydrochlorothiazide (HCTZ) 12.5 mg, telmisartan 40 mg and 80 mg is more effective than losartan/HCTZ (50/12.5 mg) at the end of the dosing interval. Furthermore, greater reductions in last 6 h mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) are achieved with telmisartan/HCTZ (80/12.5 mg) than with valsartan/HCTZ (160/12.5 mg) in obese patients with type 2 diabetes and hypertension. Recent data from a large group of patients show that telmisartan 80 mg controls the early morning blood pressure surge more effectively than ramipril 5–10 mg and, thus, may have a greater beneficial effect on long-term cardiovascular risk. This supposition is being tested in the ongoing Telmisartan alone and in combination with ramipril global endpoint trial (ONTARGET) programme.

18. **Christiano argano**[55] **et al.** studied the effects of 24 weeks losartan and ramipril treatment, both alone and in combination, on blood pressure and left ventricular

mass (LVM) and function, have been evaluated in hypertensives.57 hypertensives with stage 1 and 2 essential hypertension were included. After 4 weeks run in, a randomized double-blind, 3 arm, double dummy, independent trial was used. All patients were randomly allocated to 3 treatment arms consisting of losartan (50 mg/daily), ramipril (5 mg/daily), and combined (losartan 50 mg/ramipril 5 mg/daily) for 24 weeks. LVM, LVM/h and other echocardiographic measurements, BUN, creatinine and clearance and potassium were determined after run in and 24 weeks.All groups were comparable for gender, age, BMI, BP and LVM. The prevalence of baseline left ventricular hypertrophy (LVH) was not significantly different among 3 groups. At the end of treatment, a significant ($p<0.05$) reduction in SBP, DBP, MBP, LVM and LVM/h were observed in all groups. The absolute and percent reductions in LVM/h were significantly higher in combined than losartan or ramipril groups and also in hypertensives with LVH. No significant change in absolute and percent reduction of SBP, DBP and MBP were found.These data indicate an additional cardioprotective effect of dual blockade of RAS in hypertensive patients with and without left ventricular hypertrophy.

19. **Farsang C**[56] **et al.** suggested that antihypertensive agents are widely used to reduce the risk of cardiovascular events partly beyond that of blood pressure-lowering. In particular, the angiotensin II receptor blockers (ARBs), which antagonize the vasoconstrictive and proinflammatory/pro-proliferative effects of angiotensin II, have been shown to be cardio vascularly protective and well tolerated. Although the eight currently available ARBs are all indicated for the treatment of hypertension, they have partly different pharmacology, and their pharmacokinetic and pharmacodynamic properties differ. ARB trials for reduction of cardiovascular risk can be broadly categorized into those in patients with/without hypertension and additional risk factors, in patients with evidence of cardiovascular disease, and in patients with severe cardiovascular disease, such as heart failure. These differences have led to their indications in different populations. For hypertensive patients with left ventricular

hypertrophy, losartan was approved to have an indication for stroke prevention, while for most patients at high-risk for cardiovascular events, telmisartan is an appropriate therapy because it has a cardiovascular preventive indication. Other ARBs are indicated for narrowly defined high-risk patients, such as those with hypertension or heart failure. Although in one analysis a possible link between ARBs and increased risks of cancer has surfaced, several meta-analyses, using the most comprehensive data available, have found no link between any ARB, or the class as a whole, and cancer. Most recently, the US Food and Drug Administration completed a review of the potential risk of cancer and concluded that treatment with an ARB medication does not increase the risk of developing cancer. This review discusses the clinical evidence supporting the different indications for each of the ARBs and the outstanding safety of this drug class.

20. **Bodh I Jugdut**[57] **et al.** proposed that elderly patients (age≥65 years) with hypertension are at high risk for vascular complications, especially when diabetes is present. Antihypertensive drugs that inhibit the renin-angiotensin system have been shown to be effective for controlling blood pressure in adult and elderly patients. Importantly, renin-angiotensin system inhibitors were shown to have benefits beyond their classic cardioprotective and vasculoprotective effects, including reducing the risk of new-onset diabetes and associated cardiovascular effects. The discovery that the renin-angiotensin system inhibitor and angiotensin II type 1 (AT_1) receptor blocker, telmisartan, can selectively activate the peroxisome proliferator-activated receptor-γ provides the unique opportunity to prevent and treat cardiovascular complications in high-risk elderly patients with hypertension and new-onset diabetes. Two large clinical trials, ONTARGET (Ongoing telmisartan alone in combination with ramipril global endpoint trial) and TRANSCEND (Telmisartan Randomized Assessment Study in ACE-I intolerant subjects with cardiovascular disease) have assessed the cardioprotective and antidiabetic effects of telmisartan. The collective data suggest that telmisartan is a

promising drug for controlling hypertension and reducing vascular risk in high-risk elderly patients with new-onset diabetes.

21. **Werner c**[58] **et al.** suggested that the combined use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers posses a dilemma to clinicians. On the one hand, indirect evidence from compelling, but still surrogate outcome measures such as blood pressure and proteinuria suggest some merits of this combination. On the other hand, the outcome benefits of the ACEIs+ARBs combination in morbidity/mortality trials remain confined to patients with severe congestive heart failure (CHF) and reduced ejection fraction. Incidentally, most of the benefit offered by the ACEIs+ARBs combination in these patients was not driven by mortality, but by fewer rehospitalizations for CHF. Even in patients with renal disease and proteinuria, the combined use of ACEIs and ARBs, although highly effective in reducing urinary protein excretion, has not yet been proven to significantly delay end-stage renal disease and the need for dialysis. In the Ongoing Telmisartan Alone and In Combination With Ramipril Global Endpoint Trial (ONTARGET), the dual blockade of the renin angiotensin system did not produce additional outcome benefit over that afforded by ACE inhibition alone. Notably, however, patients with BP >160/100 mmHg at entry were excluded from ONTARGET, thus limiting the applicability of these results to the treatment of hypertension. The European Society of Hypertension guidelines do not suggest large-scale use of the ACEIs+ARBs combination in patients with hypertension. However, patients with resistant hypertension, particularly if proteinuria coexists, could benefit from this combination, which however requires close monitoring for adverse events, including hyperkalemia and worsening renal function.

22. **Zou Z**[59] **et al.** proposed that Telmisartan and angiotensin-converting enzyme inhibitors are both effective and widely used antihypertensive drugs targeting renin-angiotensin-aldosterone system. The study aimed to estimate the efficacy and tolerability of telmisartan in comparison with different ACEIs as

monotherapy in the treatment of hypertension. Cochrane Central Register of Controlled Trials, PubMed and Embase were searched for relevant studies. A meta-analysis of all randomized controlled trials fulfilling the predefined criteria was performed. A random-effect model was used to account for heterogeneity among trials. Twenty-eight randomized controlled trials involving 5157 patients were ultimately identified out of 721 studies. Telmisartan had a greater diastolic blood pressure (DBP) reduction than enalapril (weighted mean difference (WMD) 1.82, 95% confidence interval (CI) 0.66-2.99), ramipril (WMD 3.09, 95% CI 1.94-4.25) and perindopril (WMD 1.48, 95% CI 0.33-2.62). Telmisartan also showed a greater DBP response rate than enalapril (relative risk (RR) 1.15, 95% CI 1.05-1.26), ramipril (RR 1.34, 95% CI 1.11-1.61) and perindopril (RR 1.22, 95% CI 1.05-1.41). There was no statistical difference in DBP reduction or therapeutic response rate between telmisartan and lisinopril (WMD -0.30, 95% CI -0.65 to 0.05; RR 0.99, 95% CI 0.80-1.23, respectively). Telmisartan had fewer drug-related adverse events than enalapril (RR 0.57, 95% CI 0.44-0.74), ramipril (RR 0.44, 95% CI 0.26-0.75), lisinopril (RR 0.70, 95% CI 0.56-0.89) and perindopril (RR 0.52, 95% CI 0.28-0.98). The meta-analysis indicates that telmisartan provides a superior BP control to ACEIs (enalapril, ramipril and perindopril) and has fewer drug-related adverse events and better tolerability in hypertensive patients.

23. **Luis M. Ruilope[60] et al.**suggested that Cardiovascular disease places a significant burden on healthcare providers. High blood pressure is the single most prevalent risk factor for CVD worldwide and is responsible for more deaths than any other risk factor. 'Cardiovascular high-risk patients' make up the broad cross-section of patients in the middle of the risk spectrum for CVD progression that is referred to as the CV continuum and includes those with atherothrombotic disease, those with target organ damage associated with type 2 diabetes and those with multiple risk factors. Angiotensin II is involved in

CVD progression at every stage of the CV continuum, making the renin–angiotensin system a rational target for pharmacologic intervention. Angiotensin II receptor blockers offer a better tolerated alternative to angiotensin converting enzyme inhibitors, with greater long-term adherence. The ARB telmisartan recently received an indication for CV prevention.

24. **Yves Lacourcière**[61] **et al.** proposed that Blood pressure has a circadian pattern with a morning surge that is associated with an increased risk of acute coronary and cerebrovascular events. In a prospective, randomized, open-label, blinded-endpoint, parallel-group, multicenter, forced-titration study of telmisartan and ramipril, the efficacy of both drugs on mean ambulatory diastolic BP (DBP) and systolic BP (SBP) during the last 6 h of a 24-h dosing interval was evaluated. Telmisartan 80 mg was consistently more effective than ramipril 10 mg in reducing both DBP and SBP during the last 6 h of the dosing interval, a measure of the early morning period when patients are at greatest risk of life-threatening cardiovascular and cerebrovascular events. Telmisartan 80 mg was also more effective than ramipril 10 mg in reducing BP throughout the entire 24-h dosing interval. Both drugs were well tolerated.

25. **Deirdree A Lan**[62] **et al.** suggested that Peripheral arterial disease (PAD) causes considerable morbidity and mortality. Hypertension is a risk factor for PAD. Treatment for hypertension must be compatible with the symptoms of PAD. Controversy regarding the effects of beta-blockade for hypertension in patients with PAD has led many physicians to stop prescribing beta-blockers. Little is known about the effects of other classes of anti-hypertensive drugs in the presence of PAD Four studies were included. Two compared ACE inhibitors against placebo. In the HOPE study there was a significant reduction in the number of cardiovascular events in 168 patients receiving ramipril (OR 0.72, 95% confidence interval 0.58 to 0.91). In the second trial using perindopril in a small numbers of patients, there was a marginal increase in claudication distance but no change in ankle brachial

pressure index (ABPI) and a reduction in maximum walking distance.The third trial in patients undergoing angioplasty suggested that the calcium antagonist verapamil reduced restenosis, although this was not reflected in the maintenance of a high ABPI. Another small study demonstrated no significant difference in arterial intima-media thickness with men receiving the thiazide diuretic hydrochlorathiazide compared to those receiving the alpha-adrenoreceptor blocker doxazosin.Evidence on various anti-hypertensive drugs in people with PAD is poor so that it is unknown whether significant benefits or risks accrue from their use. Lack of data specifically examining outcomes in PAD patients should not detract from the compelling evidence of the benefit of treating hypertension and lowering blood pressure.

26. **Anna A**[63] **et al.** suggested that Ramipril improves cardiovascular outcome in patients with peripheral arterial disease; however, the precise mechanisms of benefit remain to be elucidated. The effect of ramipril on large-artery stiffness in patients with peripheral arterial disease was examined. In addition, they determined the effect of ramiprilat on extracellular matrix from human aortic smooth muscle cell culture. 40 patients with peripheral arterial disease were randomized to receive ramipril, 10 mg once daily or placebo for 24 weeks. Arterial stiffness was assessed globally via systemic arterial compliance and augmentation index (carotid tonometry and Doppler velocimetry), and regionally via carotid–femoral pulse wave velocity. Angiotensin-converting enzyme inhibition increased arterial compliance by 0.10±0.02 mL/mm Hg, ($P<0.001$, all probability values relative to placebo) and reduced pulse wave velocity by 1.7±0.2 m/s ($P<0.001$), augmentation index by 4.1±0.3% ($P<0.001$), and systolic blood pressure by 5±1 mm Hg ($P<0.001$). Ramipril did not reduce mean arterial pressure significantly compared with placebo ($P=0.59$). In cell culture, ramiprilat decreased collagen deposition by >50% and increased elastin and fibrillin-1 deposition by >3- and 4-fold respectively. Fibrillin-1 gene expression was increased 5-fold). Ramiprilat also reduced gene and protein expression of both matrix metalloproteinase (MMP)-2 and MMP-3.

In conclusion, ramipril promoted an elastogenic matrix profile that may contribute to the observed clinical reduction in large-artery stiffness and carotid pressure augmentation, which occurred independently of mean arterial blood pressure reduction in patients with peripheral arterial disease.

27. **Hisatoshi Bekki**[64] **et al.** proposed that there is accumulating evidence that blood pressure control significantly reduces the risk of future cardiovascular events in patients with essential hypertension. However, strict BP control is often difficult to maintain, and half of hypertensive patients fail to attain BP goals on single-drug therapy. Therefore, current guidelines recommend combinations of drugs that have complimentary mode of actions for treatment of patients with moderate hypertension. In this study, they examined in hypertensive patients uncontrolled by the combination treatment with 5 mg amlodipine plus 80 mg valsartan or 8 mg candesartan whether additional BP lowering could be achieved by switching to 5 mg amlodipine plus 40 mg telmisartan. Forty-seven patients with essential hypertension who failed to achieve a target BP level by the treatment of 5 mg amlodipine plus 80 mg valsartan or 8 mg candesartan for at least 2 months were enrolled. Replacement of valsartan or candesartan by telmisartan showed a significant reduction in both mean clinic systolic and diastolic BP at 4, 8 and 12 weeks; BP level decreased from 143.7/82.3 mmHg at baseline to 135.4/77.5 mmHg at 12 weeks. Furthermore, in 8 patients of valsartan group, switching to telmisartan significantly reduced central BP by 11.8 mmHg. Our present study suggests that combination therapy with telmisartan plus amlodipine may be more beneficial than valsartan or candesartan plus amolodipine treatment for controlling brachial and central BP, which could lead to more favourable cardiovascular outcomes with this drug combination.

28. **Böhm M**[65] **et al.** proposed that Clinical trials have shown the efficacy of angiotensin II receptor blockers (ARBs) in patients with hypertension and have suggested that ARBs are noninferior to angiotensin-converting enzyme (ACE) inhibitors in patients with ischemic heart disease and heart failure. The Heart

Outcomes Prevention Evaluation (HOPE), a landmark study in high cardiovascular risk management, demonstrated the cardioprotection of the ACE inhibitor ramipril. Thus, in the recent Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET®) ramipril was selected as a comparator when exploring the cardioprotective potential of telmisartan in the first head-to-head comparison of an ACE inhibitor and an ARB in a broad cross-sectional cohort of cardiovascular high-risk patients. ONTARGET showed that telmisartan is as effective as ramipril in the management of these patients but is better tolerated. The combination of ramipril and telmisartan did not confer a further benefit but did bring about an increased rate of adverse events such as renal dysfunction. In previous ARB outcome trials, cardiovascular risk profile, nature and severity of the underlying cardiovascular disease, dosing regimens and concomitant therapies, follow-up, and endpoints have varied greatly so that caution is warranted in extrapolating evidence gained from high-risk patients to other conditions such as acute myocardial infarction or chronic heart failure.

29. **Yusuf S[66] et al.** studied that Randomized, controlled trials involving about 150,000 patients have convincingly demonstrated that angiotensin-converting–enzyme (ACE) inhibitors reduce rates of death, myocardial infarction, stroke, and heart failure among patients with heart failure, left ventricular dysfunction, previous vascular disease alone, or high-risk diabetes.ACE inhibitors do not block the production of all angiotensin II, so direct receptor blockade might be more effective. ACE inhibitors reduce bradykinin degradation, which enhances vasodilatation, but increase the rates of angioedema and cough. In patients with heart failure, angiotensin II levels may increase and symptoms worsen, despite the use of ACE inhibitors. The use of an angiotensin-receptor blocker (ARB), as compared with placebo, reduced the rate of death or hospitalization for heart failure in patients with a low ejection fraction and heart failure who either could not tolerate an ACE inhibitor or were already receiving one. As compared with beta-blockers, ARBs also reduced vascular events in high-risk patients with hypertension and left ventricular hypertrophy. Nevertheless, in

other high-risk populations, the role of ARBs as an alternative or in addition to ACE inhibitors to prevent cardiovascular outcomes is not known,.They evaluated whether the ARB telmisartan was not inferior to the ACE inhibitor ramipril and whether a combination of the two drugs was superior to ramipril alone as a treatment to prevent vascular events in high-risk patients who had cardiovascular disease or diabetes mellitus but did not have heart failure. We used a dose of ramipril that had previously been shown to be effective for this outcome.

30. **Celik T**[67] **et al.** suggested that Prolongation of P-wave times and increase of P-wave dispersion (PWD) were shown to be independent predictors of atrial fibrillation (AF). Angiotensin II receptor blockers (AARBs) and angiotensin-converting enzyme inhibitors (ACEIs) have beneficial effects on atrial conduction times. However, there are not enough data about the comparative effects of those drugs on PWD.They aimed to compare the effects of telmisartan and ramipril on PWD after 6-month treatment in hypertensive patients. Telmisartan has a much greater lowering effect on PWD and Pmaximum values than ramipril. This finding may be important in the prevention of AF in hypertensive patients.

31. **Zimmermann M**[68] **et al** .proposed that Hypertension is one of the most important modifiable risk factors for cardiovascular pathology, such as atherosclerosis and cardiac left ventricular hypertrophy, including acute events such as stroke and myocardial infarction (MI). In particular, the risk of ischaemic and haemorrhagic stroke is directly and continuously related to high blood pressure levels. The renin-angiotensin system (RAS) plays an important role in volume homeostasis and blood pressure regulation. It also helps to prevent cell and organ damage from ischaemia during acute volume loss. However, angiotensin-II (A-II)the main effector peptide of the RAS also exerts a number of pathological effects, which are mediated by the AT 1 receptor. The Ongoing Telmisartan alone and in Combination with Ramipril Global End point Trial (ONTARGET) programme consists of two parallel trials where

ONTARGET as a large, long-term study compares the efficacy of the angiotensin-receptor antagonist, telmisartan, the renin-angiotensin-converting enzyme (ACE) inhibitor, ramipril and combination therapy with telmisartan plus ramipril for reducing cardiovascular and cerebral risk. Telmisartan, due to its long duration of action, compares favourably with other angiotensin-receptor antagonists. In the Heart Outcomes Prevention Evaluation (HOPE) study, ramipril was shown to reduce the risk for MI and other cardiovascular events in patients at high risk for pathological cardiac events, but without heart failure or a low ejection fraction. The cardiovascular outcomes of high-risk patients using the same criteria as those of the HOPE study will be assessed in both trials. TRANSCEND differs from ONTARGET in that this trial will enrol patients who do not tolerate ACE inhibitors. This parallel study will therefore be able to compare telmisartan and placebo treatment. Both ONTARGET and TRANSCEND trials feature the same primary composite end point: death caused by cardiovascular disease, acute MI, stroke and hospitalisation because of congestive heart failure. The secondary end points will focus on reductions in the development of Type 2 diabetes mellitus, nephropathy, cognitive decrease and dementia as well as atrial fibrillation.

AIM AND OBJECTIVES

AIM:

The aim is to compare inflammatory mediated response and antihypertensive efficacy of ramipril and telmisartan in acute coronary syndrome patients.

OBJECTIVES:

- To asses inflammatory mediated response of ramipril and telmisartan by comparing high sensitivity c-reactive protein (hs-CRP) levels.
- To find out clinical efficacy of ramipril and telmisartan in lowering of the blood pressure.

METHODOLOGY

Design of study

Randomized, Prospective study.

Location of the study

This study was carried out in the department of cardiology of Meenakshi Mission Hospital and Research center, Madurai .

Duration of the study

Duration of the study-8 months (June 2011-february2012).

Sample size

90 Patients were entrolled in the study. Among these 43 patients are taking ramipril 5mg/OD and 47 patients are taking telmisartan 40mg/OD.

Inclusion criteria

1 .Male or female patients between the age 20-80 years.

2. Patients with clinical evidence of acute coronary syndrome.
3. Patients having BP above 140/90 mm/hg at initial treatment.

Exclusion criteria

1. Patients with congestive heart failure.
2. Patients having left ventricular dysfunction.
3. Patients having MI or stroke ≤3 weeks before study.
4. Patients with upper respiratory tract infections and acute illness.
5. Patients with acute infection and trauma.
6. Patients with clinically apparent inflammatory conditions such as rheumatoid arthritis or lupus.
7. Patients with Blood pressure less than 140/90 mm/hg at initial treatment.
8. Secondary hypertension or malignant hypertension.
9. Patients known to be hypersensitive to ramipril or telmisartan.
10. Patients having history of serious adverse drug reactions to ACE inhibitors or angiotensin receptor blockers.
11. Patients with renal dysfunction.

12. Patients receiving combination therapy.
13. Patients receiving any other investigational drug.
14. Patients with irregular follow up.

Monitoring parameters

A. Blood pressure.

B. High sensitivity c-reactive protein (hs-CRP).

Work strategy

Acute coronary syndrome patients with hypertension were enrolled for this study. Totally 90 patients were categorized into 2 groups (Group A, Group B). Group A (43 patients) are receiving Ramipril 5mg/day and Group B (47patients) are receiving Telmisartan 40mg/ day. Clinical evaluation regarding age,gender,social habits and evaluation of complications like dyslipidemia , diabetes mellitus were done in each case.

Before treatment with ramipril or telmisartan hs-CRP (HIgh sensitivity c-reactive protein) test was done. After 90 days of treatment again hs-crp test was done to evaluate inflammatory mediated response. Blood pressure were monitored at 4^{th},8^{th} and 12^{th} week of treatment. BP was monitored for 2 times at 10 minutes interval to get correct measurement of BP. The observed parameters are finally evaluated to compare the efficacy of one drug over other.

Statistical Tools

The information collected regarding all the selected cases were recorded in a master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2010)** developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

OBSERVATIONS AND RESULTS

Group A : Ramipril (43 cases) & Group B: Telmisartan (47 cases)

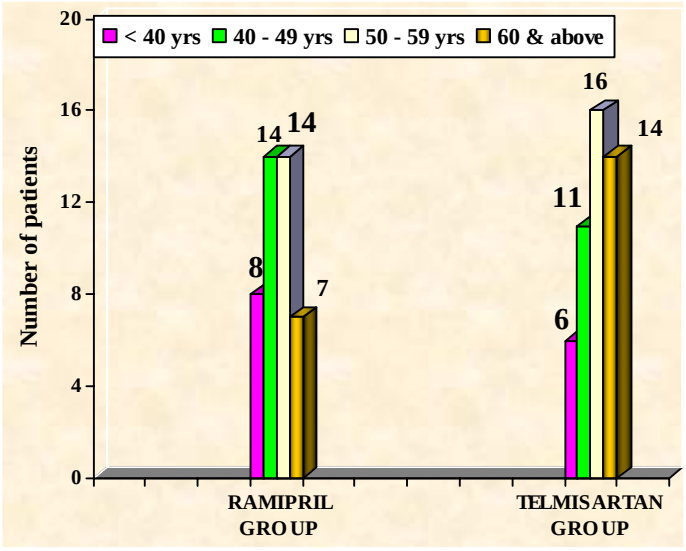
AGE GROUP DISTRIBUTION:

TABLE NO 1 : AGE GROUP DISTRIBUTION

Age group	Group A (Ramipril)		Group B (Telmisartan)	
	Number of patients	Percentage	Number of patients	Percentage
Less than 40 years	8	18.6	6	12.8
40-49 years	14	32.6	11	23.4
50-59 years	14	32.6	16	34.0
60 and above	7	16.3	14	29.8
Total	43	100	47	100
Range	32-77 years		33-79 years	
Mean	50.7 years		54.3 years	
SD	12.2 years		12.0 years	
'p' value	0.1381 Not significant			

When statistical analysis was done ,P value obtained was 0.1381.So there was no statistically significant difference observed in age distribution between two study groups

FIG NO 1 : AGE GROUP DISTRIBUTION



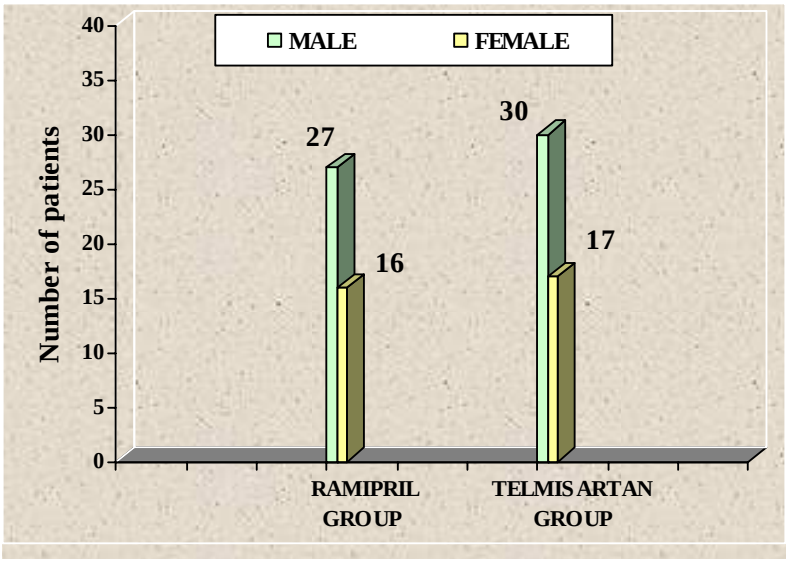
SEX DISTRIBUTION:

TABLE NO 2 : SEX DISTRIBUTION

Sex	Group A (Ramipril)		Group B (Telmisartan)	
	Number of patients	Percentage	Number of patients	Percentage
Male	27	62.8	30	63.8
Female	16	37.2	17	36.2
Total	43	100	47	100
'p' value	0.907 Not significant			

When statistical analysis was done ,P value obtained was 0.907. So statistically significant difference was not observed in sex distribution between two study groups

FIG NO 2 : SEX DISTRIBUTION



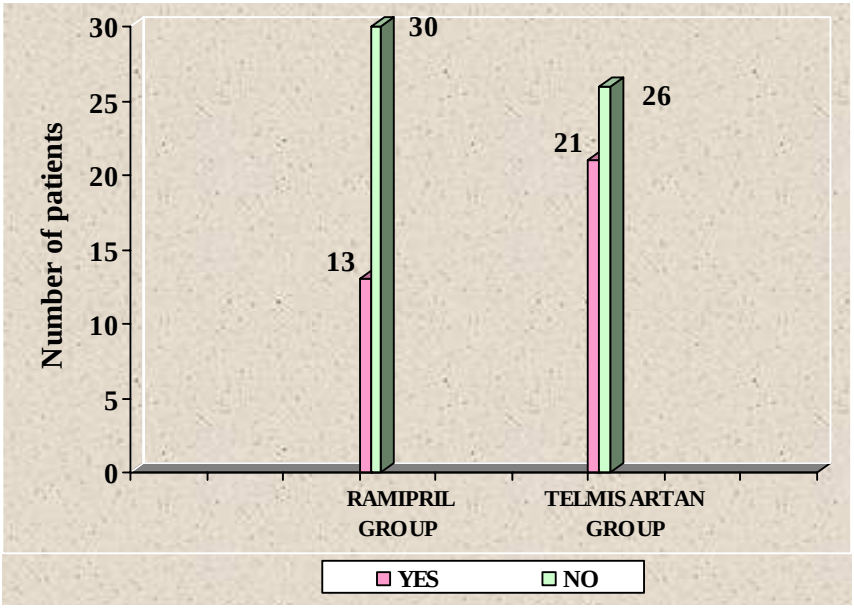
FAMILY HISTORY OF HYPERTENSION:

TABLE NO 3 : FAMILY HISTORY OF HYPERTENSION

Family History of hypertension	Group A (Ramipril)		Group B (Telmisartan)	
	Number of patients	Percentage	Number of patients	Percentage
Yes	13	30.2	21	44.7
No	30	69.8	26	55.3
'p' value	0.2323 Not significant			

Statistically significant difference was not observed in family history of hypertension in both study groups since P value obtained was 0.2323.

FIG NO 3 : FAMILY HISTORY OF HYPERTENSION



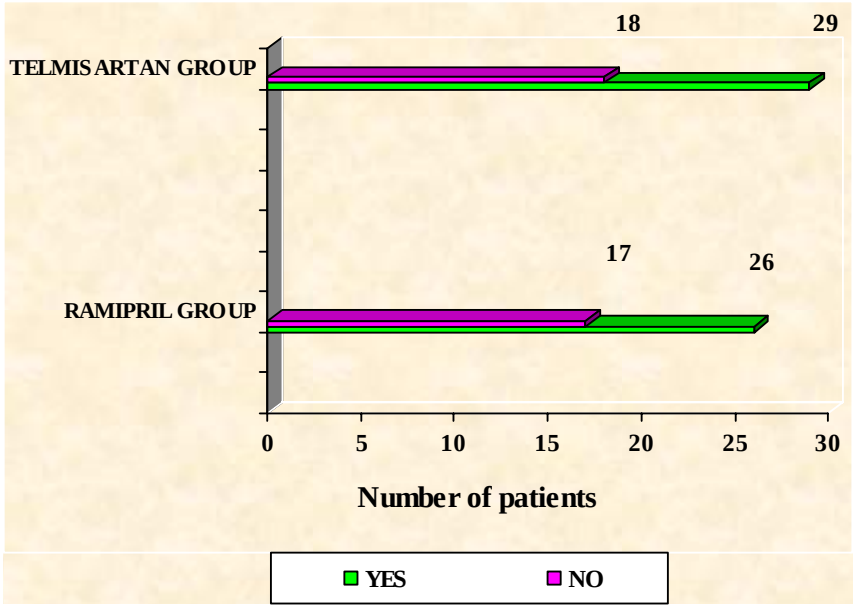
FAMILY HISTORY OF DIABETES:

TABLE NO 4 : FAMILY HISTORY OF DIABETES

Family History of diabetes	Group A (Ramipril)		Group B (Telmisartan)	
	Number of patients	Percentage	Number of patients	Percentage
Yes	26	60.5	29	61.7
No	17	39.5	18	38.1
'p' value	0.9334 Not significant			

Statistically significant difference was not observed in family history of diabetes among two treatment groups since P value obtained was 0.9334.

FIG NO 4: FAMILY HISTORY OF DIABETES



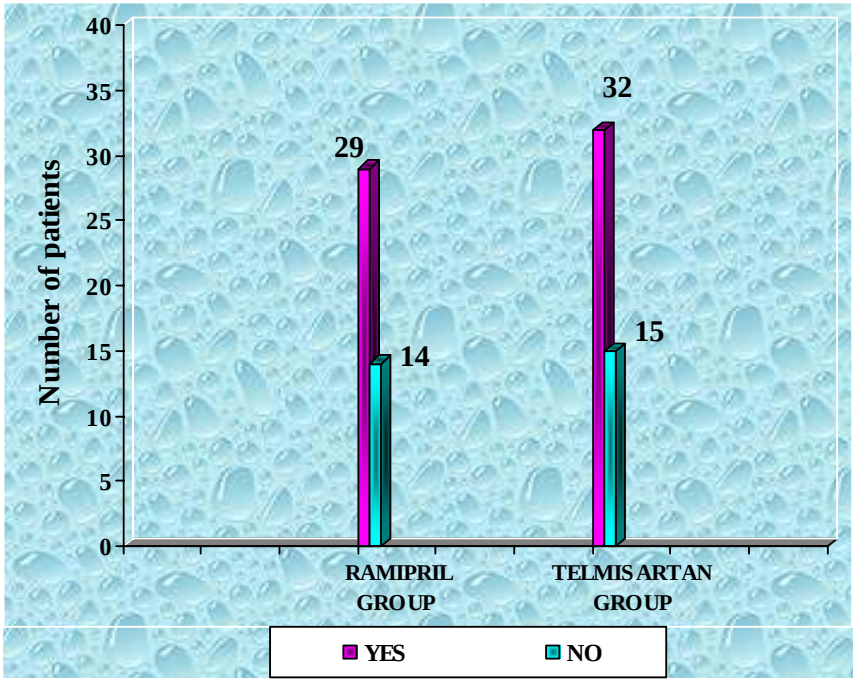
FAMILY HISTORY OF DYSLIPIDEMIA:

TABLE NO 5 : FAMILY HISTORY OF DYSLIPIDEMIA

Family History of dyslipidemia	Group A (Ramipril)		Group B (Telmisartan)	
	Number of patients	Percentage	Number of patients	Percentage
Yes	29	67.4	32	68.1
No	14	32.6	15	31.9
'p' value	0.8724 Not significant			

Statistically significant difference was not observed in family history of dyslipidemia among both study groups since P value obtained was 0.8724.

FIG NO 5 : FAMILY HISTORY OF DYSLIPIDEMIA



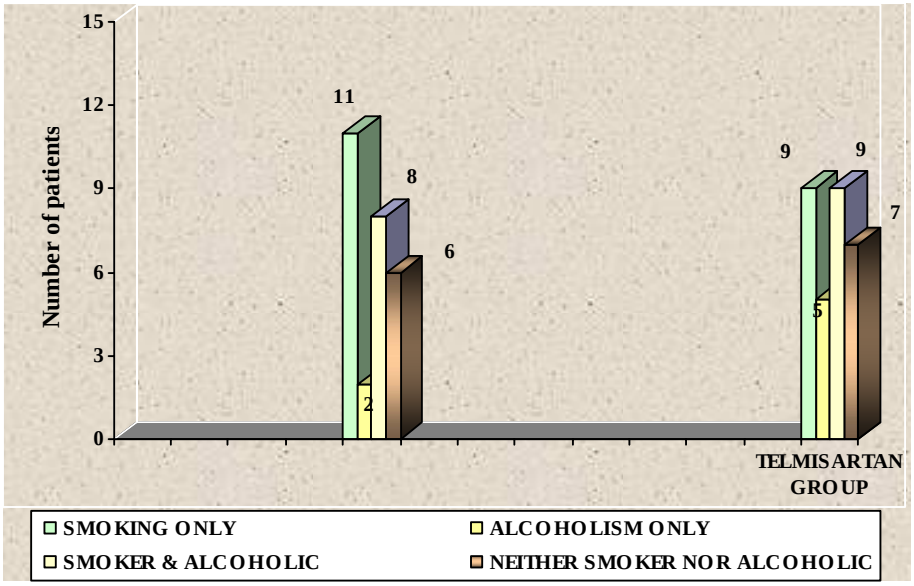
SOCIAL HABITS OF MALE PATIENTS:

TABLE NO 6 : SOCIAL HABITS OF MALE PATIENTS

Social habits	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Number of patients	Percentage	Number of patients	Percentage	
Smoker	11	40.7	9	30	0.5584 Not significant
Alcohol	2	7.4	5	16.7	0.2576 Not significant
Smoker + alcoholic	8	29.6	9	30	0.7953 Not significant
Non smoker & Non Alcoholic	6	22.2	7	23.3	0.8288 Not significant

Statistically significant difference was not observed in social habits of male patients among two study groups since P values obtained are >0.05 .

FIG NO 6: SOCIAL HABITS OF MALE PATIENTS



MEDICAL HISTORY OF DIABETES AND DYSLIPIDEMIA:

TABLE NO 7 : MEDICAL HISTORY OF DIABETES AND DYSLIPIDEMIA

Medical history	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Number of patients	Percentage	Number of patients	Percentage	
Diabetes	7	16.3	10	21.3	0.7373 Not significant
Dyslipidemia	17	39.5	11	23.4	0.1549 Not significant
Diabetes + dyslipidemia	19	44.2	26	55.3	0.3986 Not significant

Statistically significant difference was not observed in medical history of diabetes and dyslipidemia among two study groups since P values obtained are > 0.05 .

FIG NO 7: MEDICAL HISTORY OF DIABETES AND DYSLIPIDEMIA

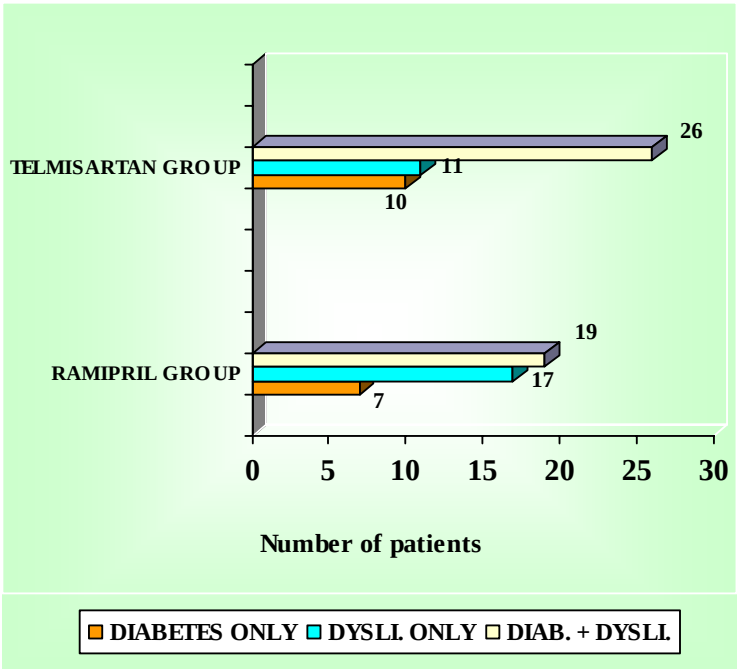


TABLE NO 8 : hs–CRP LEVEL OF PATIENTS BEFORE AND AFTER TREATMENT

hS–CRP (mg/L)	GROUP A (Ramipril)		GROUP B (Telmisartan)		'p' value
	Mean	SD	Mean	SD	
Before treatment	16.7	4.7	17.3	4.4	0.4476 Not significant
After treatment (After 90 days)	4.9	0.7	1.6	0.8	0.0001 Significant

Statistically significant difference was observed in hs-CRP level of patients after treatment with both groups since P value obtained was 0.0001.

FIG NO 8 : hs–CRP LEVEL OF PATIENTS BEFORE AND AFTER TREATMENT

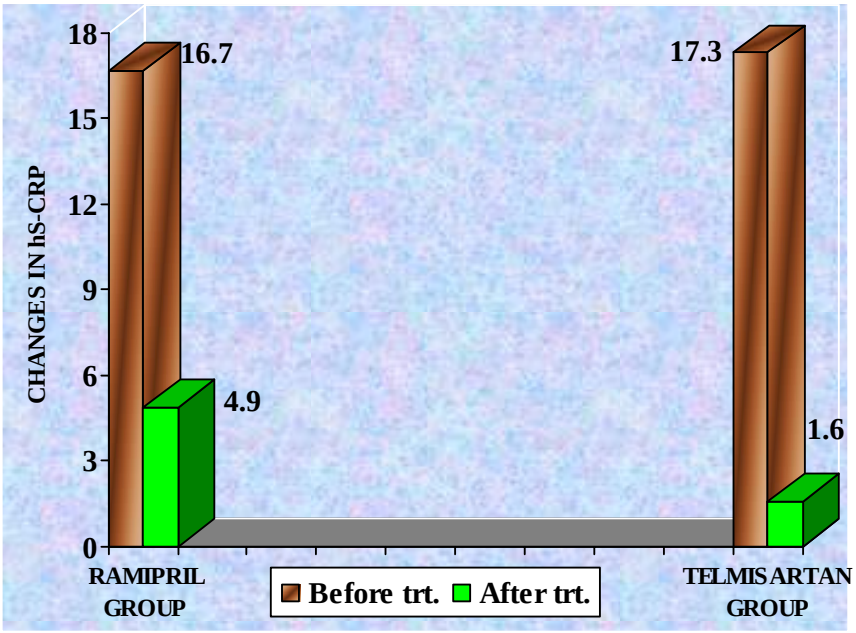


TABLE NO 9 : CHANGES IN hs-CRP LEVEL AFTER TREATMENT

hS – CRP (mg/L)	GROUP A (Ramipril)		GROUP B (Telmisartan)		'p' value
	Mean	**SD**	**Mean**	**SD**	
Change in 90 days	11.8	4.1	15.8	3.7	**0.0001 Significant**
% of change in 90 days	69.2	5.5	91.5	3.0	**0.0001 Significant**

Statistically significant difference was observed in change in hs-CRP level of patients after treatment with both groups since P values obtained are < 0.05 .

FIG NO 9 : PERCENTAGE CHANGES IN hs-CRP LEVEL AFTER TREATMENT

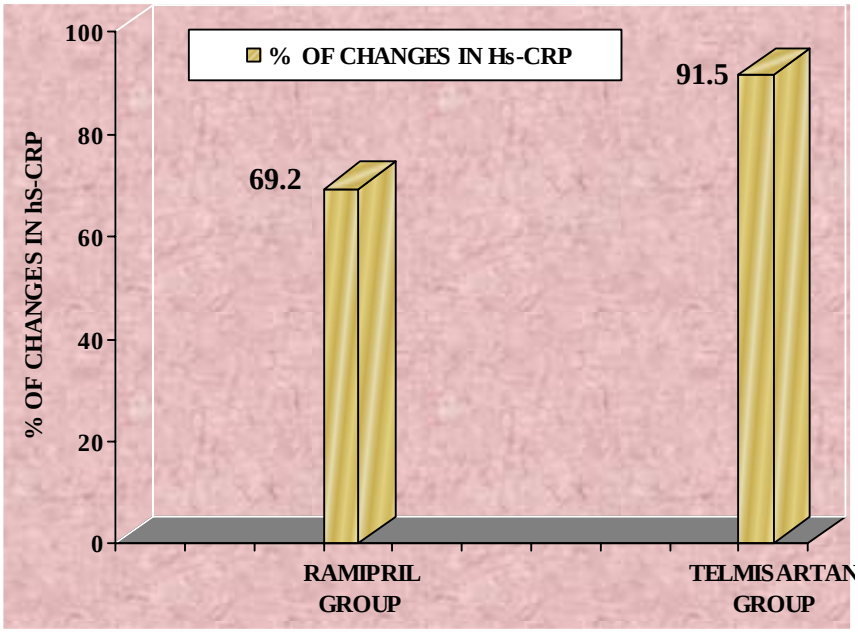


TABLE 10 : SYSTOLIC BP OF PATIENTS DURING VISIT 1

(Before treatment)

Systolic BP (mm/hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Mean	S.D.	Mean	S.D.	
Visit (1) (Before treatment)	161.6	10.3	159.8	10.2	0.4076 Not significant

Statistically significant difference was not observed with systolic BP of patients before treatment with both groups since P value obtained was 0.4076 .

FIG 10 : SYSTOLIC BP OF PATIENTS DURING VISIT 1

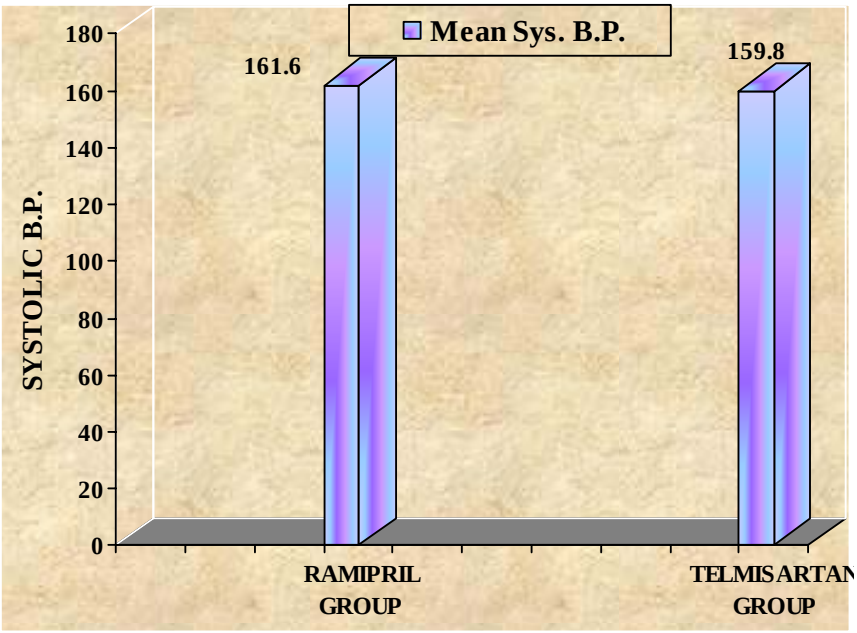


TABLE:11 SYSTOLIC BP OF PATIENTS DURING VISIT 2 (4^{TH}WEEK)

Systolic BP (mm/hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Mean	S.D.	Mean	S.D.	
Visit 2 (4^{th} week)	146.2	7.9	144.8	9.0	0.3529 Not significant
Changes at visit 2 (4^{th} week)	15.4	6.3	15.0	6.1	0.98 Not significant
% of changes at visit 2 (4^{th} week)	9.4	3.5	9.3	3.5	0.7029 Not significant

Statistically significant difference was not observed in systolic BP of patients after treatment with both groups for 4 weeks, since P values obtained were > 0.05.

FIG 11 : PERCENTAGE CHANGES IN SYSTOLIC BP OF PATIENTS DURING VISIT 2 (4^{TH} WEEK)

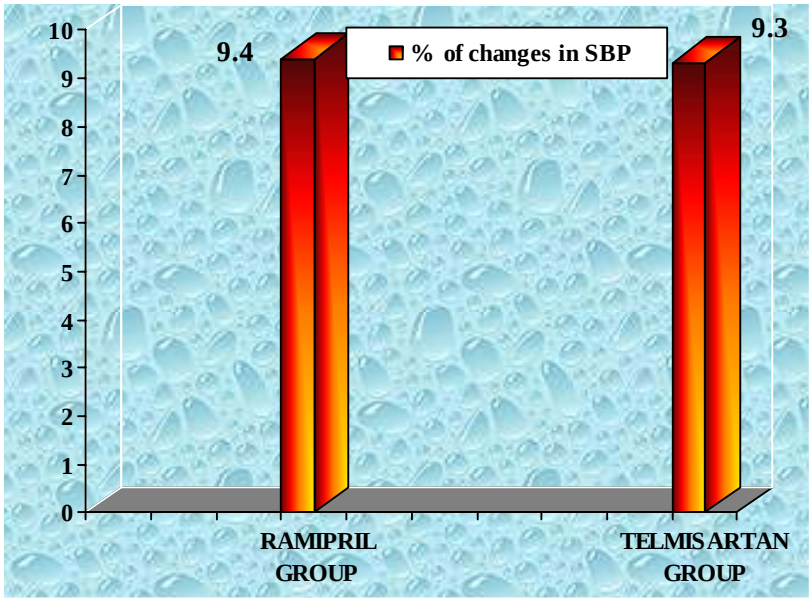


TABLE 12 : SYSTOLIC BP OF PATIENTS DURING VISIT 3 (8^{TH} WEEK)

Systolic BP (mm/hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Mean	S.D.	Mean	S.D.	
Visit 3 (8^{th} week)	137.7	7.2	130.9	9.7	**0.0014 Significant**
Changes at visit 3 (8^{th} week)	23.9	9.3	28.9	11.9	**0.0278 Significant**
% of changes at visit 3 (8^{th} week)	14.6	5.0	17.9	6.8	**0.0088 Significant**

Statistically significant difference was observed with systolic BP of patients after treatment with both groups for 8 weeks , since P values obtained were < 0.05.

FIG 12 : PERCENTAGE CHANGES IN SYSTOLIC BP OF PATIENTS DURING VISIT 3 (8^{TH} WEEK)

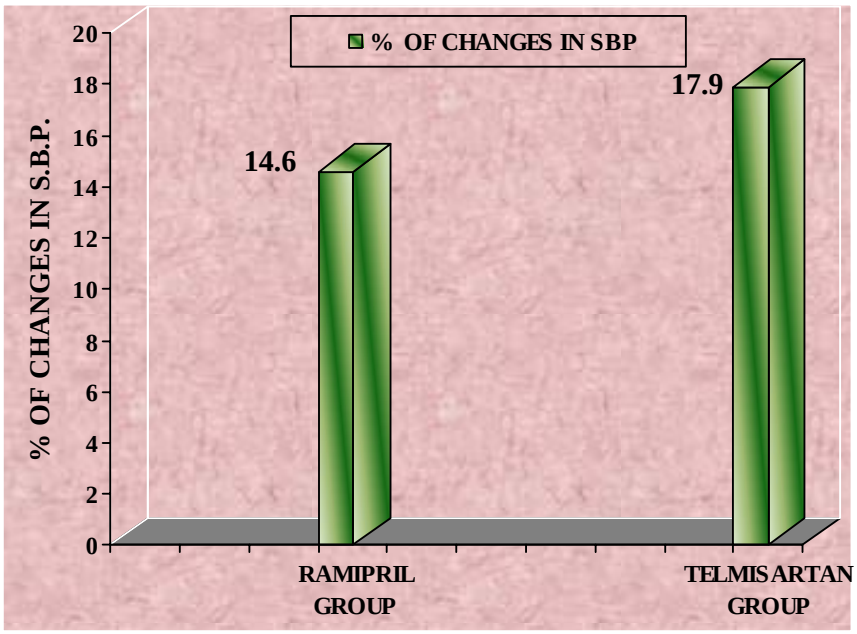


TABLE 13 : SYSTOLIC BP OF PATIENTS DURING VISIT (4)

(12TH WEEK)

Systolic BP (mm/hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Mean	S.D.	Mean	S.D.	
Visit 4 (12th week)	130.5	6.9	116.4	8.2	**0.0001 Significant**
Changes at visit 4 (12th week)	31.1	9.6	43.4	13.7	**0.0001 Significant**
% of changes at Visit 4 (12th week)	19.1	5.0	26.8	7.2	**0.0001 Significant**

Statistically significant difference was observed in systolic BP of patients after treatment with both groups for 12 weeks , since P values obtained were <0.05.

FIG 13 : PERCENTAGE CHANGES IN SYSTOLIC BP OF PATIENTS DURING VISIT (4) (12TH WEEK)

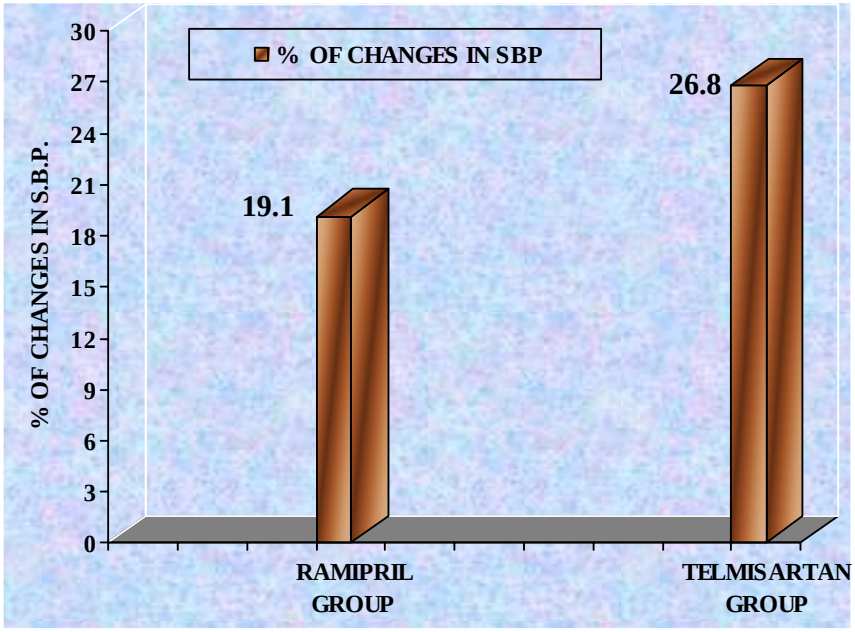


TABLE 14 : DIASTOLIC BP OF PATIENTS DURING VISIT 1

(BEFORE TREATMENT)

Diastolic BP (mm/hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Mean	S.D.	Mean	S.D.	
Visit 1 (Before treatment)	94.7	6.5	96.6	6.2	0.3369 Not significant

Statistically significant difference was not observed in diastolic BP of patients before treatment with both groups since P value obtained was 0.3369.

FIG 14 : DIASTOLIC BP OF PATIENTS DURING VISIT 1(BEFORE TREATMENT)

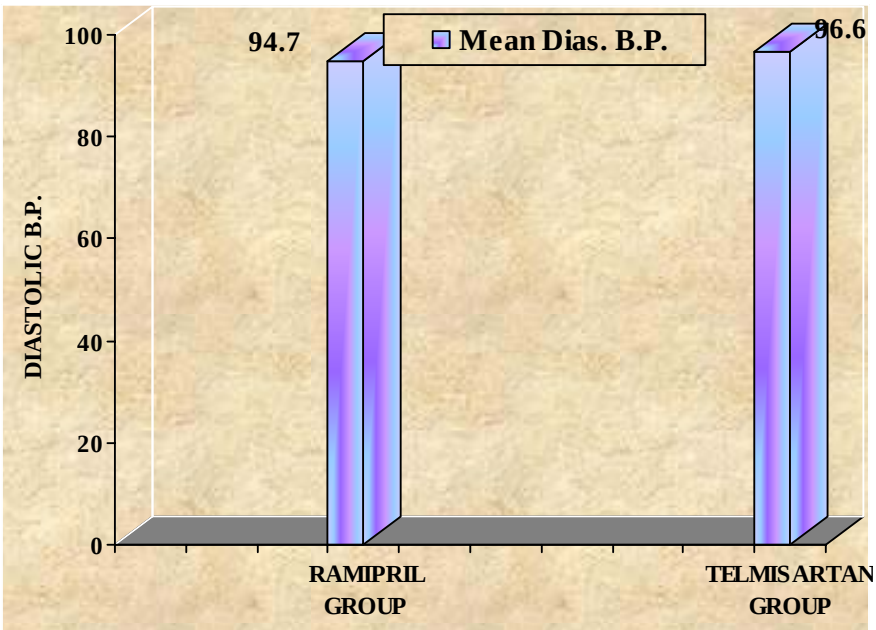


TABLE 15: DIASTOLIC BP OF PATIENTS DURING VISIT 2 (4TH WEEK)

Diastolic BP (mm/hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Mean	S.D.	Mean	S.D.	
Visit 2 (4th week)	88.1	6.3	90.3	6.5	0.0872 Not significant
Changes at visit 2 (4th week)	6.5	4.6	6.3	5.2	0.4611 Not significant
% of changes at visit 3 (8th week)	6.8	4.8	6.4	5.2	0.366 Not significant

Statistically significant difference was not observed in diastolic BP of patients after treatment for 4 weeks with both groups, since P values obtained were > 0.05.

FIG 15: PERCENTAGE CHANGES IN DIASTOLIC BP OF PATIENTS DURING VISIT 2 (4TH WEEK)

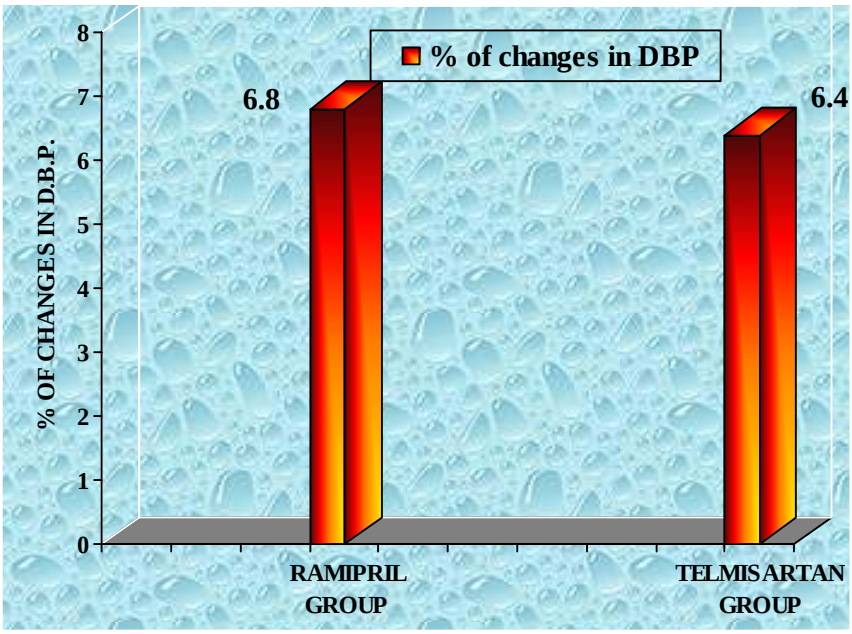


TABLE 16 : DIASTOLIC BP OF PATIENTS DURING VISIT 3 (8TH WEEK)

Diastolic BP (mm/hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Mean	S.D.	Mean	S.D.	
Visit 3 (8th week)	87.0	6.4	82.3	6.0	**0.0015 Significant**
Changes at visit 3 (8th week)	7.7	5.9	14.3	8.0	**0.0001 Significant**
% of changes at visit 3 (8th week)	7.9	6.0	14.5	7.6	**0.0001 Significant**

Statistically significant difference was observed in diastolic BP of patients after treatment for 8 weeks with both groups, since P values obtained were< 0.05.

FIG 16 : PERCENTAGE CHANGES IN DIASTOLIC BP OF PATIENTS DURING VISIT 3 (8TH WEEK)

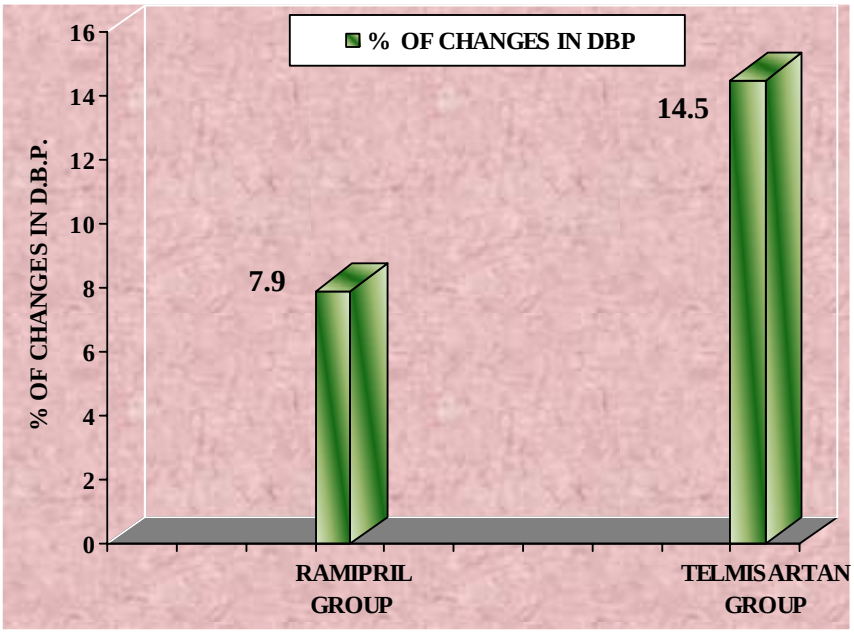


TABLE 17 : DIASTOLIC BP OF PATIENTS DURING VISIT 4 (12TH WEEK)

Diastolic BP (mm/ hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' Value
	Mean	S.D.	Mean	S.D.	
Visit 4 (12th week)	83.5	5.3	80.2	6.1	**0.0106 Significant**
Changes at visit 4 (12th week)	11.2	7.0	16.4	8.1	**0.0026 Significant**
% of changes at Visit 4 (12th week)	11.5	6.9	16.7	7.5	**0.0011 Significant**

Statistically significant difference was observed with diastolic BP of patients after treatment for 12 weeks with both groups,since P values obtained were< 0.05.

FIG 17 :PERCENTAGE CHANGES IN DIASTOLIC BP OF PATIENTS DURING VISIT 4 (12TH WEEK)

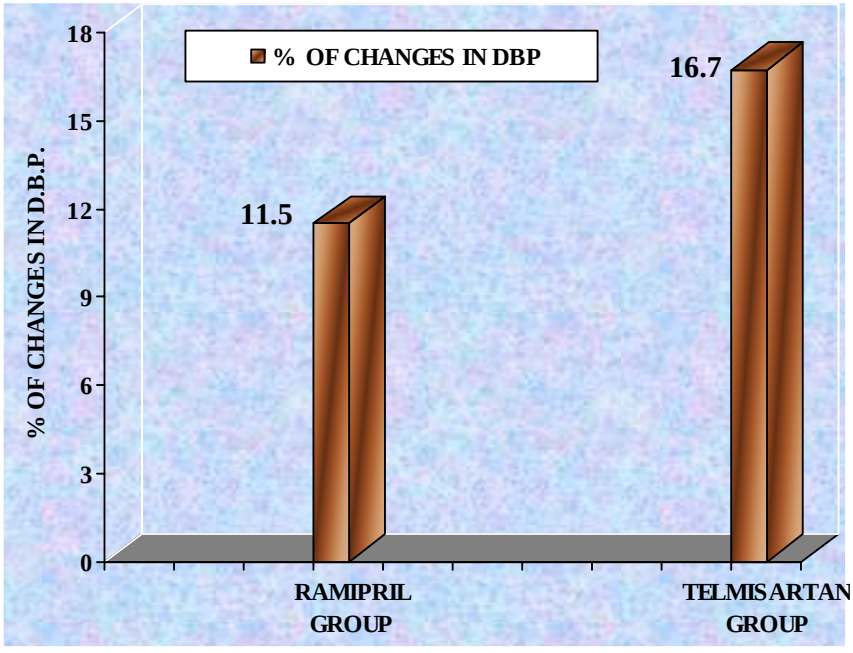


TABLE 18 : AGE AND PERCENTAGE OF CHANGES IN SYSTOLIC BP

Age group	Group A (Ramipril)		Group B (Telmisartan)	
	Mean	**SD**	**Mean**	**SD**
< 60 years	18.1	4.4	25.3	7.2
> 60 years	23.7	5.6	30.4	6.1
'p' value	**0.0254 Significant**		**0.032 Significant**	

In age and percentage changes in systolic blood pressure, P values obtained with group A and group B are < 0.05. So statistically significant difference was obsersved between two treatment groups.

FIG 18 : AGE AND PERCENTAGE OF CHANGES IN SYSTOLIC BP

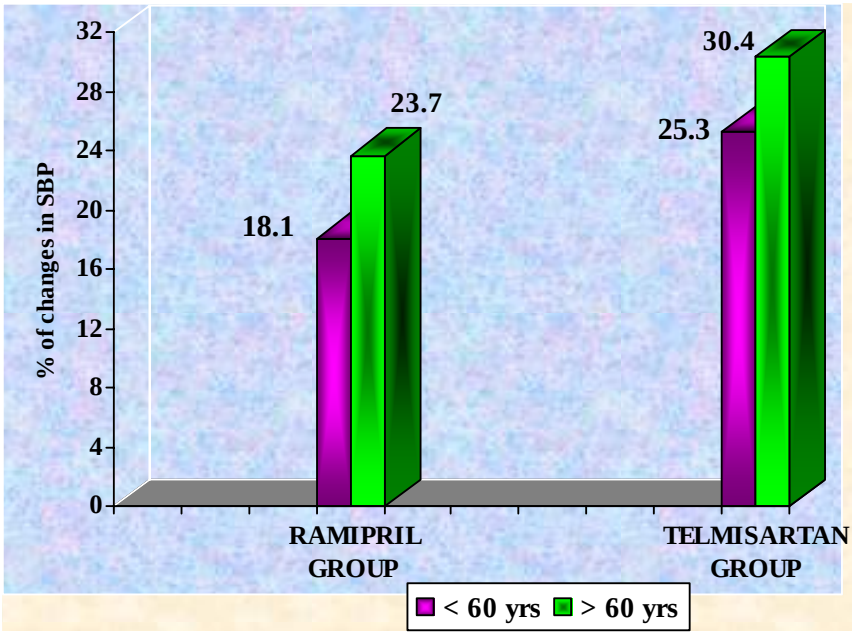


TABLE 19 : SEX AND PERCENTAGE OF CHANGES IN SYSTOLIC BP

Sex	Group A (Ramipril)		Group B (Telmisartan)	
	Mean	**SD**	**Mean**	**SD**
Male	20.3	5.0	29.5	6.0
Female	17.0	4.4	22.1	6.8
'p' value	**0.0485 Significant**		**0.0013 Significant**	

In sex and percentage changes in systolic BP ,P values obtained with group A and group B are <0.05.So statistically significant difference was observed between two treatment groups.

FIG 19 : SEX AND PERCENTAGE OF CHANGES IN SYSTOLIC BP

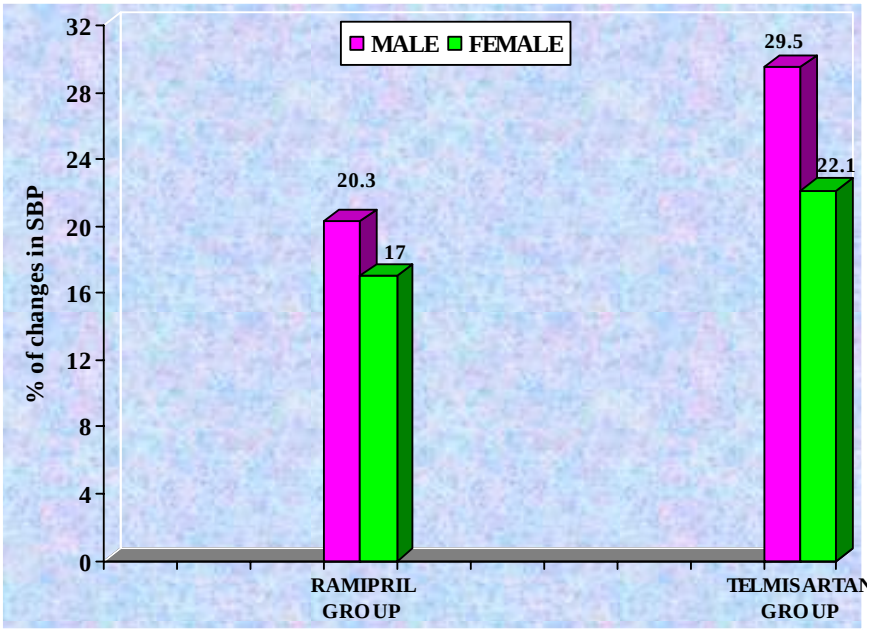


TABLE 20 : AGE AND PERCENTAGE OF CHANGES IN DIASTOLIC BP

Age group	Group A (Ramipril)		Group B (Telmisartan)	
	Mean	SD	Mean	SD
< 60 years	10.7	6.5	12.4	7.1
> 60 years	15.7	7.9	17.4	8.6
'p' value	**0.0408 Significant**		**0.037 Significant**	

In age and percentage changes in diastolic blood pressure, P values obtained with both groups are < 0.05. So statistically significant difference was observed between both treatment groups.

FIG 20 : AGE AND PERCENTAGE OF CHANGES IN DIASTOLIC BP

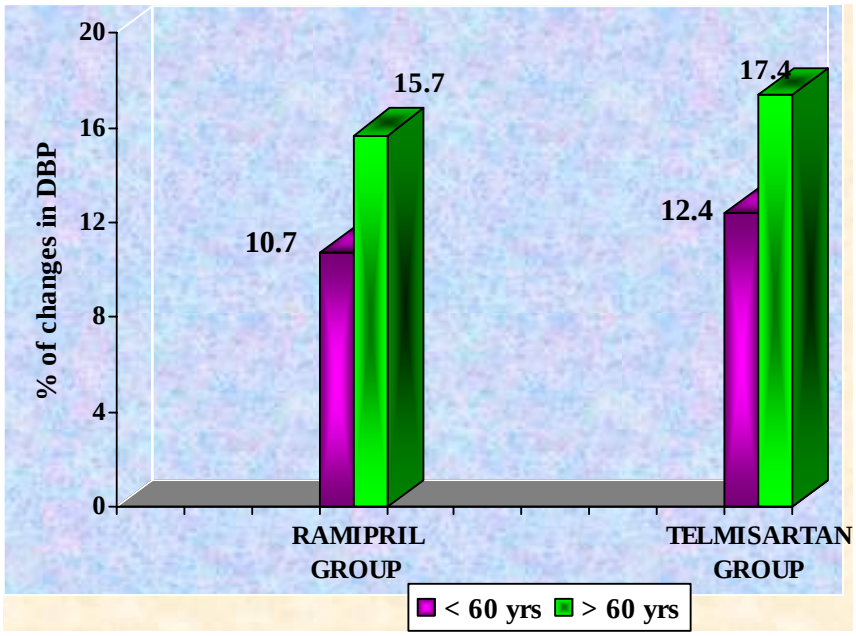


TABLE 21 : SEX AND PERCENTAGE OF CHANGES IN DIASTOLIC BP

Sex	Group A (Ramipril)		Group B (Telmisartan)	
	Mean	**SD**	**Mean**	**SD**
Male	12.8	7.4	19.0	7.1
Female	9.3	5.5	12.7	6.5
'p' value	**0.0431 Significant**		**0.0029 Significant**	

In sex and percentage changes in diastolic blood pressure, P values obtained with both groups are < 0.05. So statistically significant difference was observed between both treatment groups.

FIG 21 : SEX AND PERCENTAGE OF CHANGES IN DIASTOLIC BP

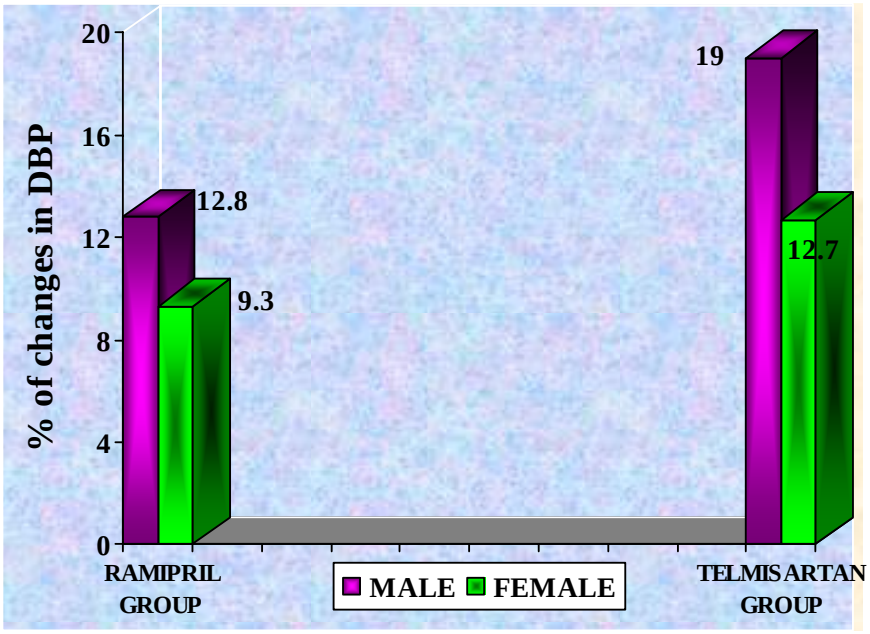


TABLE 22:OVERALL CHANGES IN SYSTOLIC BP

SYSTOLIC BP (mm/hg)	Group A (Ramipril)		Group B (Telmisartan)		'p' value
	Mean	**SD**	**Mean**	**SD**	
Baseline	161.6	10.3	159.8	10.2	0.4076 Not significant
4th week	146.2	7.9	144.8	9.0	0.3529 Not significant
8th week	137.7	7.2	130.9	9.7	**0.0014 Significant**
12th week	130.5	6.9	116.4	8.2	**0.0001 Significant**
Change in 12 weeks	31.1	9.6	43.4	13.4	**0.0001 Significant**
% of change in 12 weeks	19.1	5.0	26.8	7.2	**0.0001 Significant**

Statistically significant difference was not observed with systolic BP of patients at 4th week since P value obtained was 0.3529. Statistically significant difference was observed with systolic BP of patients at 8th week since P value obtained was 0.0014 . Statistically significant difference was observed with systolic BP of patients at 12th week since P value obtained was 0.0001. P value obtained for changes of systolic BP in 12 weeks is 0.0001, so it was statistically significant. P value obtained for percentage of change in 12 weeks was 0.0001, so it was statistically significant.

FIG 22: OVERALL CHANGES IN SYSTOLIC BP

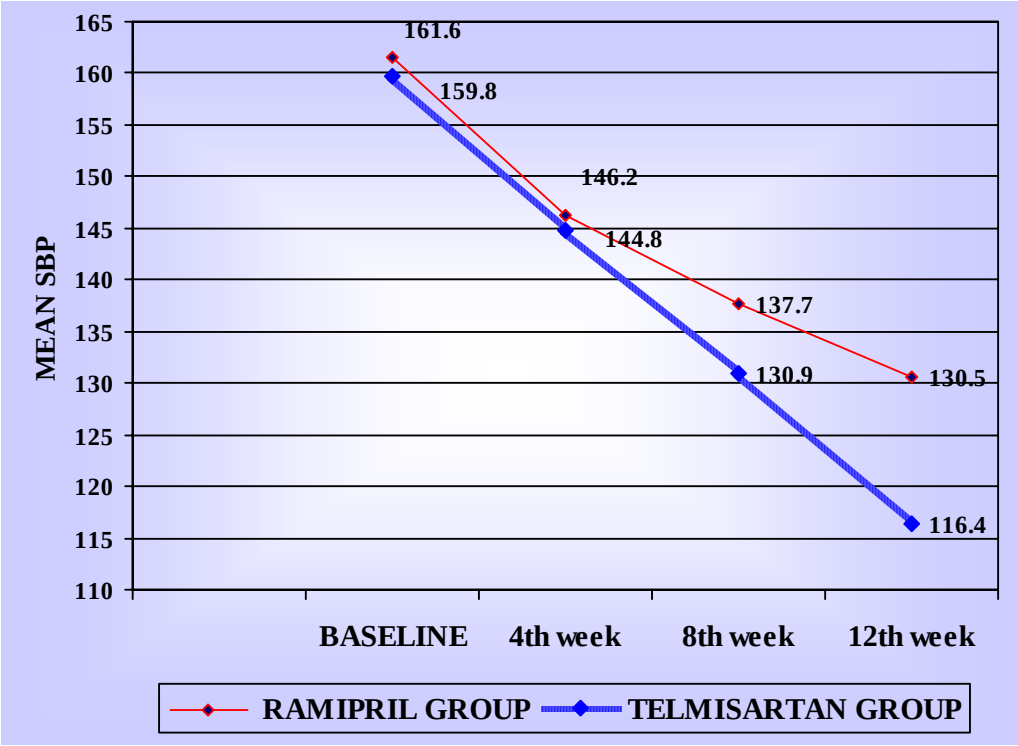
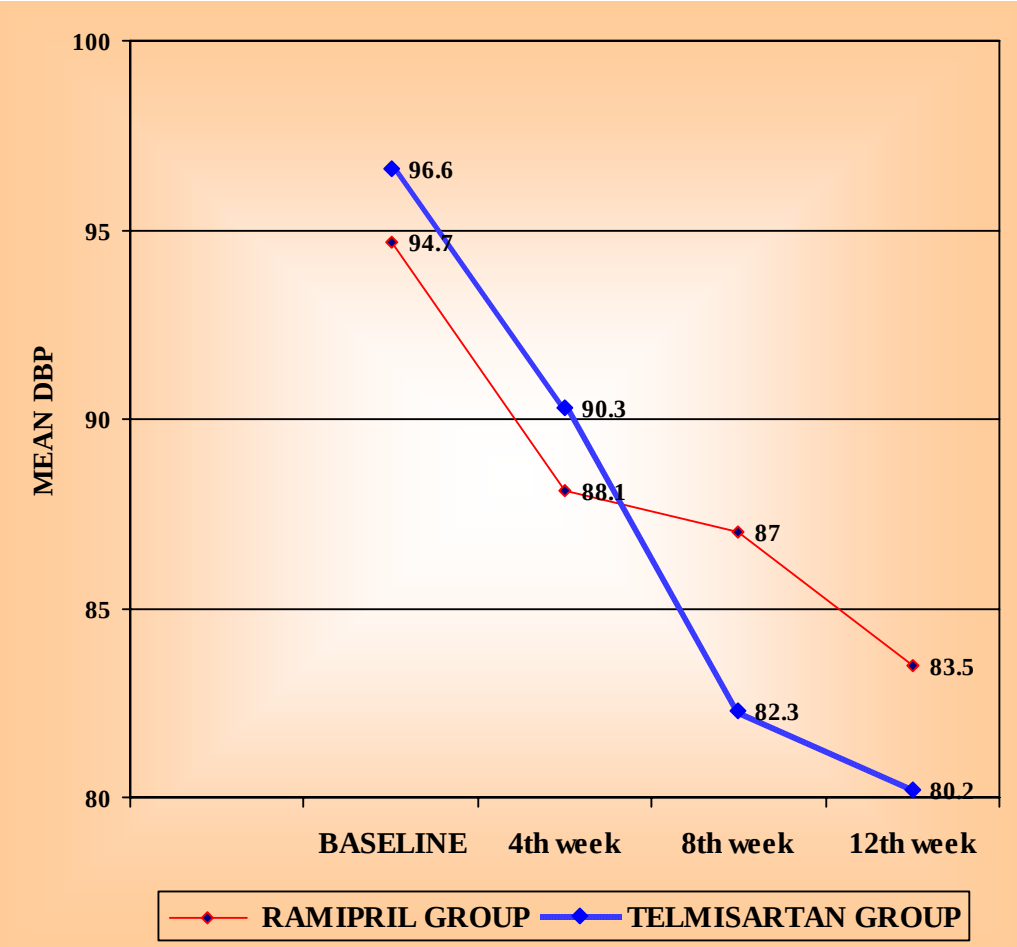


TABLE 23:OVERALL CHANGES IN DIASTOLIC BP

DIASTOLIC BP (mm/hg)	GROUPA (Ramipril)		GROUP B (Telmisartan)		'p' value
	Mean	SD	Mean	SD	
Baseline	94.7	6.5	96.6	6.2	0.3369 Not significant
4th week	88.1	6.3	90.3	6.5	0.0872 Not significant
8th week	87.0	6.4	82.3	6.0	**0.0015 Significant**
12th week	83.5	5.3	80.2	6.1	**0.0106 Significant**
Change in 12 weeks	11.2	7.0	16.4	8.1	**0.0026 Significant**
% of change in 12 weeks	11.5	6.9	16.7	7.5	**0.0011 Significant**

Statistically significant difference was not observed with diastolic BP of patients at 4th week since P value obtained was 0.3369. Statistically significant difference was observed with diastolic BP of patients at 8thweek since P value obtained was 0.0015. Statistically significant difference was observed with systolic BP of patients at 12th week since P value obtained was 0.0106. P value obtained for changes of systolic BP in 12 weeks is 0.0026, so it was statistically significant. P value obtained for percentage of change in 12 weeks was 0.0011, so it was statistically significant.

FIG 23: OVERALL CHANGES IN DIASTOLIC BP



DISCUSSION

This Study was designed to compare the inflammatory mediated response and antihypertensive efficacy of ramipril and telmisartan in acute coronary syndrome patients. In the two treatment groups ramipril 5mg/day is compared with telmisartan 40mg/day. This was a randomized prospective study done to evaluate anti-inflammatory effect by comparing high sensitivity c- reactive protein levels in acute coronary syndrome patients. Antihypertensive efficacy was evaluated by comparing regression of blood pressure among the two treatment groups.

In age group distribution, 43 cases were included in the ramipril group with age ranging from 32-77 years,their mean age was 50.7 years .In the telmisartan group 47 cases were included in the range of 33-79 years, they had a mean age of 54.3 years (Table 1).

Generally blood pressure often increases in stages. A person in their 30s may have some elevated readings that return to normal. As this person ages, the readings increase. If a person develops high blood pressure before the age of 50, his or her risk of heart attack or stroke is greatly increased. If untreated, high blood pressure can reduce duration of life by 10 or more years. Men often develop high blood pressure between the ages of 35 and 55.Women often develop high blood pressure after menopause. Increased age may often associated with a significant increase in the prevalence of hypertension and especially of systolic hypertension after age 60 years. Increased obesity between age of 30-50 years is associated with significant increases in diastolic blood pressure. Increased age is associated with an increased prevalence of secondary forms of hypertension including atherosclerotic renovascular hypertension, renal insufficiency and primary hypothyroidism. In this study there was no statistically significant difference observed between age and study groups.

In sex distribution, ramipril group contains 27 male patients and 16 female patients.Telmisartan group contains 30 male patients and 17 female patients. In this

study no significant difference was observed in the sex distribution between the two study groups (Table 2) .

Generally male patients may be more hypertensive when compared to females due to genetic factors, social habits ,stress and food habits. Hypertension is a major risk factor for stroke and cardiovascular disease. In all ethnic groups, men have higher mean systolic and diastolic blood pressure compared with women and middle age hypertension is more prevalent in men compared with women. Men are less aware and receive less treatment for hypertension compared with women. The NHANES III survey documented that only 19% of men had their blood pressure controlled. Death rates are higher in hypertensive men compared with women, and men are at greater risk for stroke, coronary heart disease, heart failure, and renal failure [69]. Coronary artery disease develops at significantly younger ages in men, thus risk factor modification and treatment should begin early in life. Men are at greater risk for sleep-related disorders that may contribute to the pathogenesis of hypertension. It is important to diagnose such disorders because effective treatment may improve blood pressure control. In this study there was no statistically significant difference observed between sex and study groups.

In family history of hypertension, Out of 43 patients treated with ramipril, 13 cases (30.2%) have the family history of hypertension. In the case of 30(69.8%) patients hypertension have no relation with the family history. In the case of telmisartan group 21(44.7%) cases have family history of hypertension and 26(55.3%) cases doesn't have family history of hypertension (Table 3).

Generally patients with family history of hypertension may have more chances to be hypertensive. Family history of blood pressure is a risk factor for developing high blood pressure. Having one or more close family members with high blood pressure before the age of 60 means have two times the risk of having it also. A strong family history means patient has 3 or more relatives who had high blood pressure before 60. It is important to understand that a family history of high blood pressure does not mean patient will have high blood pressure, but it does increase chances. A family history of high blood pressure has been linked to other risk factors for heart disease and stroke. These factors include high cholesterol, high body fat,

and being more sensitive to the effects of salt on raising blood pressure. These risk factors can put patient at risk for future heart disease and stroke. For persons with positive family history, nutritional-hygienic recommendations to avoid overweight may be important in reducing the risk of becoming hypertensive. In this study there was no significant difference observed between two treatment groups.

In family history of diabetes , Out of 43 patients treated with ramipril , 26 patients (60.5%) have family history of diabetes and 17 patients (39.5%) doesn't have family history of diabetes. In telmisartan group 29 (61.7%) patients have family history of diabetes and 18 patients (38.1%) doesn't have family history of diabetes (Table 4).

Patients with family history of diabetes are more likely to be diabetic. Both essential hypertension and diabetes mellitus affect the same major target organs. Left ventricular hypertrophy and coronary artery disease are much more common in diabetic hypertensive patients than in patients suffering from hypertension or diabetes alone. The combined presence of hypertension and diabetes concomitantly accelerates the decrease in renal function, the development of diabetic retinopathy and the development of cerebral diseases. Lowering blood pressure to less than 130/80 mm/hg is the primary goal in the management of the hypertensive diabetic patients. Beta-blockers have been reported to adversely affect the overall risk factor profile in the diabetic patient. In contrast, calcium antagonists, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers have been reported to be either neutral or beneficial with regard to the overall metabolic risk factor profile. Combination therapy is usually required to achieve blood pressure goal in diabetic patients. The addition of aldosterone antagonists may be beneficial in patients with resistant hypertension and low levels of serum potassium. Aggressive control of blood pressure, cholesterol and glucose levels should be attempted to reduce the cardiovascular risk of diabetic hypertensive patients. In general, only 25 percent of patients with hypertension have adequate control of their blood pressure. Blood pressure goals are lower, and thus more difficult to achieve, in patients who also have diabetes. Elevated blood pressure is known to contribute to diabetic micro vascular and macro vascular complications . Fortunately, reductions in blood pressure can

decrease the risk of these complications. In this study no significant difference was observed among two treatment groups.

In family history of dyslipidemia, Out of 43 patients treated with ramipril , 29 (67.4%) patients have family history of dyslipidemia and 14 (32.6%) patients doesn't have family history of dyslipidemia. In telmisartan group 32 (68.1%) patients have family history of dyslipidemia and 15(31.9%) patients doesn't have family history of dyslipidemia (Table 5).

Familial combined hyperlipidemia (FCHL) is most common frequent lipid abnormality in humans with a 5 to 10 fold increase of early myocardial infraction. Familial combined hyperlipidemia has been proposed as the leading cause of dyslipidemia in familial dyslipidemic hypertension. FCHL status and waste circumference significantly contribute to systolic blood pressure in female FCHL relatives. Visceral adipose tissue strongly contribute to high prevalence of dyslipidemic hypertension in FCHL families. In this study no significant difference observed among the two study groups.

Out of 27 male patients in ramipril group,11 patients are smokers , 2 patients are alcoholics, 8 patients are smokers and alcoholics and 6 patients are not smokers and alcoholics. Out of 30 male patients in telmisartan group , 9 patients are smokers , 5 patients are alcoholics and 9 patients are smokers and alcoholics and 7 patients are not smokers and alcoholics (Table 6).

Prevalence of hypertension may be more in patients with smoking and alcoholism.In this study no significant difference was observed between two treatment groups in social habits of patients.

Out of 43 patients in ramipril group ,7 patients have medical history of diabetes ,17 patients have medical history of dyslipidemia and 19 patients have both. Out of 47 patients in telmisartan group ,10 patients have medical history of diabetes, 11 patients have medical history of dyslipidemia and 26 patients have both (Table 7).

Patients with medical history of dyslipidemia and diabetes are more prone to be hypertensive. Evidence suggests that hypertension may share a similar

pathophysiology with cardiovascular disease (CVD). Thus, dyslipidemia, a strong predictor of CVD, may also predict incident hypertension. Dyslipidemia may lead to the subsequent development of hypertension. Thus, plasma lipids may be useful in the identification of men at risk for hypertension. Cardiovascular disease remains the leading cause of morbidity and mortality .Two of the most prevalent and asymptomatic risk factors for coronary heart disease (CHD) are hypertension and dyslipidemia and they commonly co-exist. The CHD risk in patients with co-morbid hypertension and dyslipidemia is greater than the sum of CHD risks for hypertension and dyslipidemia when they occur alone. Although there are more treatment options available today, achieving control of these diseases is challenging. Previous studies have found control rates for hypertension around 25% while control of dyslipidemia is around 33%. In this study no significant difference was observed in medical history of dyslipedemia and diabetes between the two treatment groups.

CHANGES IN hs-CRP

In this study mean hs-CRP level of patients before treatment with both groups are 16.7mg/l and 17.3 mg/l respectively (Table 8).

After treatment with ramipril and telmisartan for 90 days mean hs-CRP level reduced to 4.9mg/l and 1.6mg/l (Table 8). Change of hs-CRP levels in 90 days are 11.8 and 15.8. Percentage of change of hs-CRP levels in 90 days are 69.2% and 91.5% for ramipril and telmisartan respectively (Table 9).

hs-CRP levels are reduced in both groups after treatment with ramipril and telmisartan for 90 days. Telmisartan showed a more significant reduction in hs-CRP level by 91.5% when compared to ramipril which shows a reduction by 69.2%. (Table9).

CHANGES IN SYSTOLIC BP

In this study mean systolic BP of patients before treatment with group A and group B were 161.6 mm/hg and 159.8 mm/hg respectively (Table 10) and after 4 weeks treatment mean systolic BP reduces to 146.2 mm/hg and 144.8 mm/hg respectively. Changes in systolic BP are 15.4 and 15.0. Percentageof change in systolic BP are 9.4% and 9.3% (Table 11).

In the 8th week, mean systolic BP reduces to 137.7 mm/hg and 130.9 mm/hg. Changes in systolic BP are 23.9 and 28.9. Percentage of change in systolic BP are 14.6% and 17.9% respectively (Table 12).

In the 12th week mean systolic BP reduces to 130.5 mm/hg and 116.4 mm/hg. Changes in systolic BP are 31.1 and 43.4. Percentage of change in systolic BP are 19.1% and 26.85% respectively (Table 13).

In 4th week no significant reduction in systolic BP was observed between two treatment groups. In 8th week and 12th week systolic BP was reduced after treatment with both groups. But more significant reduction was observed in 12th week (Table 11, Table 12,Table 13).

Reduction in systolic BP was greater with telmisartan when compared to ramipril.

CHANGES IN DIASTOLIC BP

In this study mean diastolic BP of patients before treatment with both groups are 94.7 mm/hg and 96.6 mm/hg respectively (Table 14) .

On treatment with ramipril and telmisartan for 4 weeks mean diastolic BP reduces to 88.1mm/hg and 90.3mm/hg respectively. Changes in diastolic BP are 6.5 and 6.3. Percentage changes of diastolic BP are 6.8% and 6.4% (Table 15).

In the 8th week mean diastolic BP reduces to 87.0 mm/hg and 82.3mm/hg. Changes in diastolic BP are 7.7 and 14.3. Percentage changes of diastolic BP are 7.9% and 14.5% (Table 16).

In the 12th week mean diastolic BP reduces to 83.5 mm/hg and 80.2mm/hg. Changes in diastolic BP are 11.2 and 16.4. Percentage changes of diastolic BP are 11.5% and 16.7% (Table 17).

In 4th week no significant reduction in diastolic BP was observed between two treatment groups. In 8th week and 12th week diastolic BP was reduced after treatment

with both groups. But more significant reduction was observed in 12th week (Table 15, Table 16,Table 17).

Reduction in diastolic BP was greater with telmisartan when compared to ramipril .

OVERALL CHANGES IN BLOOD PRESSURE

After 4 weeks of treatment systolic blood pressure values were 146.2±7.9 mm/hg versus 144.8±9.0 mm/hg (Table 22) and diastolic blood pressure values were 88.1±6.3 mm/hg versus 90.3±6.5 mm/hg (Table 23). No significant reduction in BP was observed between two treatment groups.

After 8 weeks of treatment systolic blood pressure values were 137.7±7.2 mm/hg versus 130.9±9.7 mm/hg (Table 22) and diastolic blood pressure values were 87.0±6.4 mm/hg versus 82.3±6.0 mm/hg (Table 23) . Significant reduction in BP was observed between two treatment groups.

After 12 weeks of treatment systolic blood pressure values were 130.5±6.9 mm/hg versus 116.4±8.2mm/hg and diastolic blood pressure values were 83.5 ± 5.3 mm/hg versus 80.2 ± 6.1mm/hg (Table 22, Table 23) . After 12 weeks of treatment ,the greater significant reduction in BP was observed in telmisartan group when compared to ramipril.

Percentage of change in systolic blood pressure in 12 weeks are 19.1±5.0 versus 26.8±7.2 and diastolic blood pressure are 11.5±6.9 versus 16.7±7.5 (Table 22, Table 23). Greater significant percentage of reduction in BP was observed in telmisartan group when compared to ramipril.

AGE AND SEX WITH HYPERTENSION

Approximately 30-40% of all people over 65 have high blood pressure. Blood pressure control reduces complications associated with hypertension and improves the quality of life among elderly people[70]. The importance of effective BP control in the elderly is heightened by the fact that they represent one of the most rapidly growing segments of the population. In the case of elderly patients, the physician will aim to

achieve a gradual reduction in blood pressure and on possible side effects[71]. With only slightly elevated blood pressure, older patients should reduce excess weight , alcohol consumption and should do appropriate physical activities, A low-sodium (salt) diet should be recommended for hypertensive patients. The prevalence significantly increased with age in both sexes. About 33% of men and 25% of women aged 45-54 years may have hypertension. About 73% of men and 64% of women aged ≥75 years or older may have hypertension[72].

Significant differences were not observed in age and sex distribution between the two groups in this study (Table 1, Table 2). Percentage changes in both systolic and diastolic blood pressure with age and sex have shown significant relationship between two treatment groups (Table 18, Table 19, Table 20, Table 21).

Patients having high blood pressure are more likely to develop coronary heart diseases. Intensive control of BP is mandatory to prevent complications associated with hypertension. Although combination therapy may be required for many high risk patients, the initial use of an effective and well tolerated agent should improve patient compliance and reduce number of steps needed to reach BP control. Life style modification has been recommended as major guide line through out the therapy of hypertension since it can effectively reduce blood pressure.

CONCLUSION

Telmisartan reduces high sensitivity c reactive protein levels to a greater extent when compared to ramipril .This study reveals telmisartan has a more potent anti-inflammatory effect than ramipril. Anti-inflammatory properties of ramipril and telmisartan may have beneficial cardiovascular effects in addition to their blood pressure lowering action.

In this study, telmisartan was consistently more effective than ramipril in reducing both systolic and diastolic blood pressure. Regression of blood pressure in acute coronary syndrome patients reduces cardiovascular risk and mortality.

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CASE RECORD FORM

Patient data:

1.Name:

2.Age:

3.Sex

4.MR no:

5.Address:

6.Ph no:

7.Drug used: Ramipril ☐ Telmisartan ☐

8.Family history

Hypertension: Yes/No

Dyslipidemia: Yes/No

Diabetes: Yes/No

9.Social habits of patients

Smoker: Yes/No

Alcoholic: Yes/No

10.Medical history

Diabetes: Yes/No

Dyslipidemia: Yes/No

On starting treatment (1st visit)

Date:

Dose of:

Parameters:

BP : SBP/DBP mm/hg

hs-CRP: mg/l

2nd visit (4thweek)

Date:

Dose of:

Parameter:

BP: SBP/DBP mm/hg

3rd visit(8th week)

Date:

Dose of:

Parameter:

BP : SBP/DBP mm/hg

4th visit(12th week)

Date:

Dose of:

Parameters:

BP: SBP/DBP mm/hg

hs-CRP: mg/l

Any other details : _____

_____

Doctor's signature